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Table of Contents.

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ORIGINAL ARTICLES— Page.

Pancreatitis at the Royal North Shore Hospital of Sydney from 1925 to 1950, by Thomas F. Rose 453

Venous Occlusion Plethysmography: II. An Aid to the Diagnosis and Management of Peripheral Vascular Disease, by Alfred J. Barnett 458

The Problem of Simple Goitre, by F. F. Rundle, M.D., F.R.C.S. 464

REPORTS OF CASES—

Abdominal Migraine: Report of a Case, by D. W. Piper, M.B., B.S. 468

A Case of Hemiparesis following Cut Throat, by John B. Nally 469

REVIEWS—

A Text-Book of Medicine 470

An Atlas of Surgical Pathology 471

Pituitary Hormones 471

Enzymes and Enzyme Systems 471

Eye Manifestations of Internal Diseases 472

An Outline of Fractures 472

BOOKS RECEIVED 472

LEADING ARTICLES—

Violent and Unexplained Deaths: Their Incidence and Investigation 473

CURRENT COMMENT—

The Action of Morphine on the Intestine 474

Erythema Nodosum 474

Myocardial Infarction in Detroit 475

ABSTRACTS FROM MEDICAL LITERATURE— Page.

Obstetrics and Gynæcology 476

BRITISH MEDICAL ASSOCIATION NEWS—

Scientific 478

OUT OF THE PAST 481

MEDICAL PRACTICE—

Pharmaceutical Benefits Act Regulations 481

CORRESPONDENCE—

Pre-Bronchiectasis 482

Poisoning from a "Benzedrine Inhaler" 482

Mortality from Congenital Malformations in Australia 482

POST-GRADUATE WORK—

The Melbourne Permanent Post-Graduate Committee 482

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA 483

AUSTRALIAN MEDICAL BOARD PROCEEDINGS—

New South Wales 483

Tasmania 484

UNIVERSITY INTELLIGENCE—

University of Melbourne 484

NOMINATIONS AND ELECTIONS 484

DIARY FOR THE MONTH 484

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 484

EDITORIAL NOTICES 484

PANCREATITIS AT THE ROYAL NORTH SHORE HOSPITAL OF SYDNEY FROM 1925 TO 1950.[1]

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IT is apparent on reviewing the literature of pancreatitis[2] in recent years that several lesions are being discussed under this title. Most authors discuss acute pancreatitis, either acute œdema of the pancreas (acute interstitial pancreatitis) or acute necrosis of the pancreas (acute hæmorrhagic pancreatitis), whose pathology, symptoms and signs are known to all. In addition, there is the clinical entity of acute or subacute recurring or relapsing pancreatitis (Priestley, 1950), characterized clinically by repeated episodes of upper abdominal pain. The physical findings are comparable with mild episodes of acute pancreatitis. A still further syndrome is that of chronic recurrent or relapsing pancreatitis (Maimon, Kirsner and Palmer, 1948; Gambill, 1951). This again is described as an entity characterized by episodes of pain in the upper part of the abdomen occurring at intervals of weeks or months, often extending over many years. The pain may be mild or severe. Steatorrhœa and raised serum and urinary enzyme values may be present, as also changes in carbohydrate metabolism.

These types are discussed almost as separate entities, and I propose to show by a review of the cases of pancreatitis occurring at the Royal North Shore Hospital of Sydney from January, 1925, through 1950, that they can be correlated, and that they are all part and parcel of the one disease process of pancreatitis.

Thus pancreatitis may show itself in an acute form, mild or severe, the attacks may be single or multiple, and in any one of them death may occur. Complete resolution may follow, or a more chronic form, characterized by fibrosis of the pancreas, may supervene. On the other hand, the disease may take a chronic form all along, the patient going progressively downhill until death ensues. Any form may give rise to pseudocyst or even to pancreatic abscess, both of which are merely episodes in this disease entity. The clinical manifestations, therefore, are protean in their behaviour.

Incidence.

There were 89 cases of pancreatitis at the Royal North Shore Hospital during this 25-year period, during which there were approximately 156,500 admissions—that is, an approximate frequency of one in 1750 admissions.

Sex and Age of Onset.

There were 65 females and 24 males. The youngest female was aged fifteen years and the youngest male was aged twenty years. The oldest female was aged eighty years and the oldest male seventy years. Seventy *per centum* of the males and 70% of the females commenced their symptoms at the age of forty years or over.

[1] The substance of a lecture given at a meeting of the Clinical Society of the Royal North Shore Hospital of Sydney on August 7, 1951.

[2] The term "pancreatitis" is retained here as it is one of traditional usage and is correct if inflammation is regarded as being the response of the body tissues to an irritant.

Types and Progress of the Disease.

The 89 cases in this study were classified as follows. Twenty were of the chronic recurrent type of pancreatitis, in five of which the lesion was localized to the head of the pancreas. These patients were followed for up to eighteen years, and six died during this time. (Pancreatic lithiasis or calcification, stigmata of chronic pancreatitis—Waugh *et alii*, 1946—was not observed.)

In 69 cases the attacks were of the acute type, 48 being due to acute œdema of the pancreas with 10 deaths. Twenty-one were due to acute pancreatic necrosis, and 15 patients died during the period of review, which in some instances extended to twenty-three years.

If these 69 acute cases are taken as a whole, (*a*) 19 patients had one attack only which resulted in death immediately or shortly afterwards, (*b*) 21 had one attack with recovery, but were unable to be followed for more than a year, (*c*) six had one attack only with recovery and were able to be followed up for over one year, one for as long as twenty-three years, and (*d*) 24 had two or more attacks. Some were followed up for sixteen years and had as many as eight attacks. Six eventually died from the disease or its complications.

Thus of the 30 patients with acute pancreatitis followed up for longer than twelve months ((*c*) and (*d*) above), 24 had more than one attack—that is, their disease was of the acute relapsing type. (This figure is higher than the 33 out of 65 cases given by Probstein, 1951, or the 18 of the 53 cases of Edlund, 1950.)

Now, can the 20 chronic cases be correlated with the 69 acute cases? Clinically, of the 24 patients with acute relapsing pancreatitis who were followed up for over twelve months, eight showed symptoms characteristic of chronic pancreatitis—namely, attacks of pain with wasting, vomiting, flatulence, steatorrhœa (one case), changes in carbohydrate metabolism (two cases) and jaundice not due to common bile duct stone (one case). However, none came to autopsy, so that the impression is a clinical one only.

Six of the 20 patients with chronic pancreatitis died, and the autopsy of two showed the usual typical pancreatic fibrosis. However, the remaining four, after episodes of chronic pancreatitis extending over three to ten years, all died in an attack of acute pancreatitis which was proved at autopsy to be due to acute pancreatic œdema with fat necrosis. Microscopically the changes of old fibrosis were seen to be overlaid by the more acute changes of œdema and necrosis of parenchymal cells.

These four cases, therefore, show that chronic pancreatitis may have an acute phase, and they furnish evidence of a link between the acute and chronic forms. Probstein (1951), strangely enough, states that he has never seen such cases and, in fact, doubts their existence. However, Gambill (1951) describes acute attacks with widespread fat necrosis occurring in chronic pancreatitis.

Results of Pancreatitis of All Types.

Death, complete resolution, abscess formation, pseudocyst formation or changes in carbohydrate metabolism may occur.

Death.

Death may occur in an acute attack, either the first (19 cases) or a later one (six cases). On the other hand, death may supervene at the end of a chronic relapsing course from pancreatic insufficiency (four cases) or from *diabetes mellitus* (two cases). Thus, of the 89 patients under discussion, 31 died in the period of review.

Complete Resolution.

It is obvious that resolution cannot take place once fibrosis of the pancreas has occurred, but it may do so after one or even more acute attacks, as is shown in the following two cases.

A patient had two attacks of acute interstitial pancreatitis in three years. Two years later still, cholecystectomy was performed for acute cholecystitis with calculi. The pancreas was normal, both macroscopically and microscopically.

The same thing occurred in another patient five years after an attack of acute hæmorrhagic pancreatitis.

Pseudocyst Formation.

Five cases were complicated by pseudocyst, three occurring in the course of chronic pancreatitis (with one death) and two after acute hæmorrhagic pancreatitis.

In the first, the cyst ruptured spontaneously into the peritoneal cavity, recovery ensuing after simple drainage of the cyst. It had not recurred three years later (Rose, 1948).

The second occurred in the tenth year of recurring chronic pancreatitis and was drained externally. Three months later, the patient died in acute diabetic coma. Autopsy revealed a shrunken, thick-walled cyst full of green semi-solid material. The pancreas was swollen and irregular, microscopic examination showing areas of acute necrosis and older fibrosis.

The third patient had acute hæmorrhagic pancreatitis treated by laparotomy only. Three months later, cholecystectomy for cholelithiasis was performed. The pancreas appeared normal. However, two years later, a pancreatic pseudocyst developed. This was drained externally with a good result.

The fourth patient had a pancreatic pseudocyst drained externally. He then developed chronic pancreatitis, proved by biopsy at laparotomy ten years later. There was then no evidence of the cyst.

The fifth patient developed acute hæmorrhagic pancreatitis, which was drained only. A large epigastric mass developed, which slowly subsided over the next two months.

Abscess Formation.

The peritoneal exudate and the pancreas were examined bacteriologically in only 15 cases, and in all were sterile. However, there were two cases of peripancreatic abscess following drainage of the gland for acute pancreatitis. One was due to *Bacterium coli* and one to Proteus, and both were in the lesser sac. The latter patient died in one month from toxæmia.

Disturbance of Carbohydrate Metabolism.

The disturbances of carbohydrate metabolism vary from transient glycosuria to full-blown diabetes, becoming progressively worse as more of the pancreas becomes involved. These disturbances are of three types: (*a*) transient temporary changes; (*b*) post-pancreatitic *diabetes mellitus*; (*c*) *diabetes mellitus* complicated by pancreatitis.

(*a*) Schumaker (1940) stated that 11% of patients with acute pancreatitis had glycosuria during some part of their acute attack, which might be only transient. Two of my cases belonged to this category. However, if glycosuria is a relatively rare finding in acute pancreatitis, hyperglycæmia is not. Broiq and Varangot (1937) collected 72 cases of acute pancreatitis and found that the fasting blood sugar level was above 150 milligrammes *per centum* in 57 cases, and in 34 of these it was over 200. They point out that though these changes are usually transient, glucose tolerance is often altered, even in mild cases of pancreatitis, but not in other cases of acute abdominal disease.

In this series routine blood sugar estimations were not made, though I think this investigation should be instituted, as it may offer some bearing on later prognosis.

(*b*) Pancreatitis, by its destructive effect on the islets of Langerhans, may be followed by *diabetes mellitus*. Warren (1948) found three cases in 16 cases of acute pancreatitis, and Nothnagel (1905) nine in 134 cases of chronic pancreatitis. In the present series this occurred in five cases, eventually causing death in two, both from diabetic coma, one following acute interstitial pancreatitis and the other three months after the drainage of a pseudocyst of chronic pancreatitis. Among the three survivors the diabetes developed during the course of chronic pancreatitis in two, and a year after an attack of acute hæmorrhagic pancreatitis in the third. Lawrence (1951) states that the diabetes in chronic pancreatitis is mostly mild, but may need insulin. However, all the surviving patients have required progressively increasing doses of insulin.

Thus this sequel to an attack of pancreatitis is common enough for the clinician to be always on the watch for it, and although Warren, Fallis and Barron (1950) found

only five cases from 1917 to 1944, they stated that it may be more common if it is looked for.

(c) On the other hand, *diabetes mellitus* itself may be complicated by pancreatitis, acute or chronic, which may be the cause of the epigastric pain from which many diabetics suffer.[1]

There were 1872 patients with *diabetes mellitus* admitted to the Royal North Shore Hospital from 1925 to 1950; 69 died, and autopsies were performed on 59. Only 20 of these had any pancreatic lesion akin to pancreatitis. Sixteen of these had fibrosis of the pancreas, which I have not included in the cases under review because the patients were all asymptomatic, and because the condition was not even the cause of death, which was due to diabetic coma. These pancreatic lesions probably belong to a different category from those causing symptoms. They appeared, in fact, to be incidental findings. Microscopic examination in most instances still showed islet cells present.

However, there was no doubt about the cause of the other four deaths. Two were due to typical acute interstitial pancreatitis and one to acute hæmorrhagic pancreatitis following the amputation of a gangrenous leg. In the fourth case a diabetic patient developed portal cirrhosis and then died in an attack of acute hæmorrhagic pancreatitis. Root (1937) reported four deaths from acute pancreatitis complicating diabetic coma in autopsies on 26 diabetics.

Three other patients with *diabetes mellitus* developed acute pancreatitis, from which all recovered. One had one attack of acute pancreatic œdema; the second had two attacks of acute hæmorrhagic pancreatitis in five years, later developing an abscess in the lesser sac, which was successfully drained; whilst the third had four attacks of acute pancreatic œdema in three years.

Schumaker (1940) states that acute pancreatitis in which *diabetes mellitus* develops carries a high mortality rate, and this is confirmed by the Royal North Shore Hospital series, in which the mortality was two in five. Schumaker also stated that the mortality is even higher in cases of *diabetes mellitus* complicated by pancreatitis. Only one of 19 of his patients survived, whereas in the present series three of seven survived.

Association of Pancreatitis with other Diseases.

Twenty-three cases of this series were unassociated with other lesions. Of the remaining 66 cases, seven were associated with *diabetes mellitus* (these have already been discussed); 47 were associated with gall-bladder disease, 35 subjects having gall-stones; six were associated with hepatitis; five followed operations for other lesions; two were associated with trauma and two with pregnancy.

Association with Gall-bladder Disease.

In the 25-year period under review, 1570 patients with cholecystitis were admitted to this hospital; 47 of these cases were associated with pancreatitis, and 13 ended fatally. Of these cases of cholecystitis, calculi were present in 1175, which were associated with 35 cases of pancreatitis, 29 acute and six chronic. In the other 395 cases no calculi were present; there were 12 cases of pancreatitis, six acute and six chronic. Thus the ratio of pancreatitis to cholelithiasis was one in 33, and so was the ratio of pancreatitis to cholecystitis without calculi. However, acute pancreatitis tended to be more frequently associated with cholelithiasis, whereas chronic pancreatitis tended to associate more with cholecystitis without stones.

If we look at the matter from another aspect, 24 cases of pancreatitis were associated with chronic cholecystitis and calculi with nine deaths, whereas 11 were associated with acute cholecystitis and calculi with two deaths. Twelve cases were associated with chronic cholecystitis with no stones and two deaths. Only two patients of the 47 had stones in the common bile duct; the stones were not impacted and the patients were symptomless.

[1] This section should be in the section on associated diseases, but it is more convenient to place it here in the disturbances of carbohydrate metabolism.

In this section may be discussed the following two interesting series of cases.

1. In Probstein's (1951) series of 65 patients with pancreatitis 11 had undergone previous cholecystectomies before their first attack. In this series of 89, six (five acute and one chronic) occurred for the first time after cholecystectomy for cholelithiasis at intervals ranging from three days to sixteen years. Two of these patients had recurrent attacks over the next four years, one eventually dying in an attack, and one developing chronic pancreatitis. The chronic cases occurred first eight years after cholecystectomy, with an attack of jaundice mimicking a stone in the common bile duct. Laparotomy confirmed the true diagnosis. Four other cases kept recurring, one for five years, even though cholecystectomy had been performed for an attack of acute pancreatitis. One of these patients even developed a pseudocyst five years after the operation. Consequently it may be seen that cholecystectomy may benefit the patient with pancreatitis if the gall-bladder is diseased, but it will not necessarily affect the course of the pancreatitis.

2. The second series was also an interesting group of five patients who presented themselves with severe epigastric pain, a tender mass in the region of the gall-bladder, and a high urinary diastase excretion varying from 200 to 800 units. As the symptoms did not subside, operation (four cholecystectomies and one cholecystostomy) was necessary in each case for the treatment of empyema of the gall-bladder due to a calculus impacted in the cystic duct. Surprisingly, however, the pancreas appeared perfectly normal and there was no fat necrosis. Biopsy was not performed, as it did not seem justifiable in the presence of the infected gall-bladder. This meant either that the gall-bladder condition could cause raised enzyme values, or that the pancreas was not so innocent as it looked. The urinary diastase figures fell to normal within four days of operation in each instance.

Four of these patients have been operated on only during the last six months, and all have so far been well. The fifth, however, developed further pain a week after the operation, and the urinary diastase value rose again to 200 units. A large mass simultaneously developed in the epigastrium and subsided in the next ten days as the urinary diastase figures fell.

The answer to the problem of the raised enzyme figures and the apparently normal pancreas can be found in this case and in the following cases, in which the patients have been observed for longer.

Five patients with similar histories, physical findings and enzyme values were operated on fourteen days after the onset of symptoms. At operation subsiding acute cholecystitis was found, together with a thickened pancreas with fat necrosis. It can be seen that the normal-looking pancreas was actually the seat of early acute pancreatitis.

Association with Hepatitis.

There is a definite association between pancreatitis and hepatitis. Firstly, just as symptomless pancreatic fibrosis is found at autopsy in subjects who have died from *diabetes mellitus*, so it may be found in chronic hepatitis or cirrhosis (I have put all types of chronic hepatitis together, following the teaching of Dible, 1951). In 115 cases of chronic hepatitis there were five deaths due to liver cirrhosis (three being due to liver insufficiency, one to rectal and one to œsophageal hæmorrhage); in all these cases symptomless pancreatic fibrosis was present, often with small cysts. These cases are not included here, as the patients were asymptomatic, and death was obviously due to the liver lesion. *En passant*, however, one of these cases is interesting.

A female subject had a splenectomy performed at the age of thirty-two years for congenital spherocytosis. She was well until twenty years later, when she had an illness of two months' duration with jaundice, breathlessness, ascites and melæna. Death ensued, and autopsy revealed a grossly fibrotic nodular liver. The pancreas was fibrotic and had many small cysts. The gall-bladder and common bile duct were normal.

However, although I have deliberately excluded these cases, chiefly on account of the liver death and the lack

of symptoms of any pancreatitis during life, nevertheless it is interesting to note that Gambill (1951) states that hepatosplenomegaly with œsophageal and gastric varices is a complication of chronic pancreatitis. However, with these excluded cases here it could quite well be the other way round.

Three cases of pancreatitis (two acute, one ending fatally, and one chronic, ending fatally) occurred in the 146 cases of acute infective hepatitis, and three cases of acute pancreatitis (one hæmorrhagic and two interstitial, one ending fatally) in the 115 cases of chronic hepatitis at the Royal North Shore Hospital from 1925 to 1950.

Post-operative Pancreatitis in Other Lesions (Except that following Gall-bladder Operations).

Three cases occurred in the post-operative period of other illnesses, and all ended fatally, as follows: (i) one from acute hæmorrhagic pancreatitis two days after suprapubic prostatectomy for simple prostatic adenoma; (ii) one from acute interstitial pancreatitis three weeks after a suprapubic cystostomy for bladder carcinoma; (iii) one two days after amputation of a gangrenous leg in a diabetic patient. As Probstein (1951) states, acute pancreatitis may be the cause of many post-operative collapses.

Trauma.

Two cases of acute pancreatitis were associated with trauma. One occurred three days after the removal of a duodenal diverticulum, which had burrowed into the pancreas. R. B. Cattell (1951) mentions a patient who died of a similar catastrophe following removal of a duodenal diverticulum. The other occurred ten years after a crushing injury to the abdomen. During the intervening period attacks of epigastric pain occurred, which culminated in acute pancreatic œdema with fat necrosis.

Pregnancy.

Two cases only had any relationship to pregnancy, although we have a large obstetric department here.

One patient had acute pancreatitis when five months pregnant and recovered, going on to full-term delivery.

The other had her first attack of acute hæmorrhagic pancreatitis three weeks after the baby was born. Three months later still a further attack occurred, for which cholecystostomy was performed after laparotomy had disclosed acute hæmorrhagic pancreatitis with chronic cholecystitis and cholelithiasis. This was followed by death from shock.

Langmade and Edmondson (1951) state that enzyme estimations performed in pregnant women with *hyperemesis gravidarum* and epigastric pain would reveal many more such instances complicating pregnancy and the puerperium.

Mortality of Pancreatitis Associated with other Diseases.

In order to judge the effect of associated disease on the mortality of pancreatitis without introducing too many complicating factors, such as different duration of follow-up periods, I have taken the immediate mortality of the first attack in those patients with acute pancreatitis. These are shown in the following tabulation:

Acute pancreatitis:

(*a*) With no associated lesion: 18 cases with four deaths.
(*b*) With gall-bladder disease: 25 cases with five deaths.
(*c*) With hepatitis: four cases with three deaths.
(*d*) With *diabetes mellitus*: four cases with two deaths.
(*e*) Following operation: two cases with two deaths.
(*f*) With multiple diseases: five cases with three deaths.

We can see immediately that associated diseases, except disease of the gall-bladder, increase the mortality very significantly. The apparent innocuousness of the diseased gall-bladder is an interesting observation.

Some Remarks on the Ætiology of Pancreatitis.

All must agree with Siler and Wulson (1950) that the answer to the question of ætiology is not yet found.

Since Long (1942) and Schwegler and Boyden (1936, 1937) have demonstrated that the sphincter of Oddi does not surround the ampulla of Vater, but only the termination of the common bile duct, we cannot blame spasm of this structure for forcing bile into the pancreas. In addition, Mann and Giordani (1923) found that at times the sphincter of Oddi also surrounded the main pancreatic duct, hence spasm would serve only to close the pancreatic duct as well. Nor can we often blame a common bile duct calculus impacted in the ampulla. Schmieden and Sebening (1928) found gall-stones in the ampulla of Vater in only 4·4% of 1200 cases of hæmorrhagic pancreatitis, and this has been confirmed since by many authors (Fallis and Plain, 1939). In the present series, in two only of the 47 cases associated with gall-bladder disease (that is, two of the total 89) were stones present in the common bile duct, and these were not impacted. Nor in any of the cases was any comment made on increased pressure in the common bile duct. Indeed, we know that acute pancreatitis may occur only in that part of the pancreas drained by the accessory pancreatic duct (of Santorini) (Aird, 1949).

We know that bile in the pancreatic duct has irritating properties; but so has any irritant (Rich and Duff, 1936). Thus the presence of bile in the pancreatic duct is not a necessary condition for the onset of pancreatitis.

Now that we have cleared away old lumber, with what can we replace it? Wainwright (1951) offers evidence to show that the main mechanical cause of acute pancreatitis is obstruction to the pancreatic ducts by epithelial metaplasia and its shedding into the lumen of the duct. The cause of this is unknown.

However, we do know that pancreatitis occurs more in relation to some diseases than to others; for instance, of the 89 patients, 23 only had no other associated disease. These 89 cases occurred in 156,500 hospital admissions—that is, an occurrence rate of one in 1750. Seven of the cases complicated 1872 cases of *diabetes mellitus*—that is, one in 268 cases, or nearly seven times the average incidence. Forty-seven cases were associated with 1570 cases of gall-bladder disease—that is, one in 33, or 53 times the average incidence. Six cases were associated with 261 cases of hepatitis—that is, one in 43, or 40 times the average incidence.

Thus there is an obvious association between pancreatitis and these diseases. Again, however, we can get pancreatitis in the virus diseases, especially mumps, and even in infantile paralysis (Green, 1951). It may follow trauma to the pancreas due to a penetrating ulcer, injuries or surgical manipulation (Warren, 1951). It may occur in association with pregnancy or after any operation.

Dick and Wallace (1928) showed that in liver failure the injection of STIPP can cause acute pancreatitis, and they postulated that as the liver is failing, the irritant dye is excreted by the pancreas. However, this theory explains only those cases associated with hepatitis, of which there were only six in this series. Consequently it is impossible to postulate a common ætiology for all cases.

Treatment.

The present vogue in treatment is conservative, with no operative interference. I have taken two groups of cases—(*a*) the 23 with no associated disease with six deaths, and (*b*) the 47 associated with gall-bladder disease with 13 deaths—to show the effects of different methods of treatment.

In comment on Table I it may be seen that there is a high mortality rate among those treated conservatively, probably mainly owing to the fact that many were extremely severe cases. Laparotomy only added no risk, nor did drainage of the pancreas. Cholecystectomy also added little to the risk. However, cholecystostomy in those cases in which a diseased gall-bladder was present had a very high mortality rate (eight in 10 cases), the cause of death being shock in five cases, pneumonia in two and renal failure in another. Thus cholecystostomy is a very undesirable operation in such cases. In other words, apart from this, mortality appears to be due to the severity of the disease and not the treatment used.

TABLE I.
Results of Various Forms of Treatment.[1]

	No Operation.	Laparotomy Only.	Drain to Pancreas.	Drain to Pancreas and Cholecystostomy.	Cholecystostomy.	Cholecystectomy.
Group (*a*): no associated disease (23 with 6 deaths)	8 (4)	6 (1)	4 (1)	1 (0)	2 (0)	2 (0)
Group (*b*): with associated disease of gall-bladder (47 cases with 13 deaths) ..	5 (2)	5 (0)	4 (1)	3 (0)	10 (8)	20 (2)
	13 (6)	11 (1)	8 (2)	4 (0)	12 (8)	22 (2)

[1] The figures in parentheses represent deaths.

When using the conservative treatment one must be sure of the diagnosis and rely on the clinical findings as well as the raised enzyme values. There may be something else requiring more active surgical interference, such as empyema of the gall-bladder, which may produce a raised enzyme value, or even a ruptured duodenal ulcer or a ruptured diverticulum of the colon (Grieg, 1950). The figures given above show that a laparotomy does not add to the danger, and it is better to be sure than sorry.

Special Diagnostic Features.

The Serum Amylase and Urinary Diastase.

The serum amylase and urinary diastase contents are estimated at the Royal North Shore Hospital by the method of Wohlgemuth (Harrison, 1947), the normal figures for the former being three to ten units and for the latter 6·6 to 50 units. Sixty units is a significant figure for the urinary diastase in pancreatitis, in which figures may vary from 60 to 2000 units. The urinary diastase test first made its appearance in the records about 1929, the serum amylase test following some years later.

Thirty-six pancreatitis patients had the urinary diastase content estimated, and 15 the serum amylase content in addition. The former estimation was found to be reliable; it does not fall so quickly as some authors maintain, reliable figures being found as late as the fourth or fifth day of illness. Probstein (1951) points out that the urinary diastase content remains raised even after the serum amylase content has fallen to normal figures.

In this series the urinary diastase figures ranged from 60 to 800 units, mostly being between 100 and 200 units. The serum amylase content was raised with them, varying from 25 to 80 units. It is seen that the height of the urinary diastase or serum amylase content does not necessarily indicate the severity of the disease; for instance, in a patient who died within twenty-four hours of acute hæmorrhagic pancreatitis, the urinary diastase content was never above 200 units. This was undoubtedly due to the widespread destruction of the pancreatic parenchyma. In acute pancreatic œdema very high figures may be produced, as the parenchymal cells are mostly preserved. Even in chronic pancreatitis the enzyme figures may go up to 200 units if the pancreatic duct is blocked enough.

The judicious use of enzyme tests in acute or subacute abdominal disease will reveal more cases of pancreatitis. For instance, Grollman *et alii* (1951) found 45 cases of acute pancreatitis in a 250-bed hospital in sixteen months. It must be remembered that a raised serum amylase content (or urinary diastase content) may occur also in epidemic parotitis, in renal failure, in pancreatic trauma, in perforation of the gastro-intestinal tract, in carcinoma of the ampulla of Vater (Miller *et alii*, 1951), or even after the exhibition of morphine (Gross *et alii*, 1951).

So far serum lipase estimations have not been carried out as a routine measure at the Royal North Shore Hospital.

Steatorrhœa.

Wirts and Snape (1951) point out that the pancreas has a large functional reserve, and a minimal amount of healthy pancreatic tissue can produce normal results to function tests. This statement applies to the presence or absence of steatorrhœa. Whereas its presence implies either a blocked pancreatic duct or extensive destruction of the pancreatic parenchyma, its absence does not necessarily indicate a normal pancreas.

Most fat in normal fæces comes from the action of bacteria in cellulose. In pancreatic steatorrhœa it is the appearance of bulky pale stools with the presence of fatty acid crystals and a high percentage of total fat that is important. The ratio of split to unsplit fat is not regarded as important nowadays.

In this series steatorrhœa was found in only one case of acute pancreatitis, when the patient had diarrhœa with bulky pale stools containing 68% total fat, 40% of which was unsplit. The patient had four attacks of acute pancreatitis in two years, each accompanied by steatorrhœa which lasted only during the attack. This patient also had mild diabetes.

Steatorrhœa was present in six of the 20 cases of chronic pancreatitis, two occurring in the convalescent period following drainage of pseudocysts.

Diagnosis.

Diagnosis of chronic pancreatitis may be extremely difficult, as it may mimic any chronic upper abdominal disease, especially gall-bladder disease, with which it is often associated (in 12 of 20 cases in this series). If the common bile duct is obstructed, then carcinoma of the head of the pancreas may be mimicked, especially if the pancreatitis is localized to the head of the pancreas. Biopsy alone may then reveal the diagnosis, and even this is not certain. In these cases the serum amylase content may be of little help, as this may rise in either disease. Most authorities state that a biopsy should always be undertaken in suspected carcinoma of the pancreas before radical surgical treatment is attempted. Many a patient with "inoperable carcinoma" of the head of the pancreas has lived for years after a cholecyst-enterostomy.

Acute pancreatitis also may mimic any acute or subacute abdominal condition, and if conservative treatment is to be used great care must be taken in the diagnosis.

Of the 69 acute cases, 32 started with the classical combination of severe pain, vomiting, tenderness, rigidity and a high urinary or serum amylase level. In a further five the additional sign of jaundice was present.

Of the 20 chronic cases, four started symptoms of pain, vomiting, flatulence and wasting. In six more jaundice was present in addition. (The two patients with stones in the common bile duct had no jaundice.)

Twelve of the acute cases started like a gall-bladder attack, two with jaundice also, and all the patients had cholelithiasis. Six cases of chronic pancreatitis also started like a gall-bladder attack (two with jaundice), and four of the patients had a diseased gall-bladder. Therefore it is not surprising that this disease may be masked by the symptoms attributable to the gall-bladder.

In two acute cases the pain commenced in the lower part of the abdomen, and another mimicked acute appendicitis so well that the appendix was removed before the pancreatitis was diagnosed.

Cyanosis occurred only once, and this in the case of spontaneous rupture of the pseudocyst. The more exotic signs like Cullen's periumbilical extravasation of blood or Grey Turner's flank-bruising were not seen.

Eight of the 69 cases started like acute intestinal obstruction with generalized abdominal distension, confirmed by X-ray examination. However, Siler and Wulson (1950) found this in 23% of their 98 cases. Grollman *et alii* (1950) describe localized paralytic ileus due to paralysis of an upper jejunal loop which can be early picked up by X-ray examination. This, together with a raised enzyme value, is said to be a diagnostic certainty. This upper jejunal loop paralysis was not seen in any of the present series.

Whereas Siler and Wulsin (1950) noticed that in 25% of their cases of acute pancreatitis a palpable epigastric mass was present, due to the swollen pancreas, it was found in only two of the 69 acute cases in the present series.

Summary.

Eighty-nine cases of pancreatitis at the Royal North Shore Hospital from 1925 to 1950 have been reviewed. It has been shown from these cases that the various syndromes of pancreatitis (acute relapsing and chronic) are able to be correlated and are part and parcel of the one disease entity. The various sequelæ are discussed, and also the association of pancreatitis with other diseases, especially *diabetes mellitus*, gall-bladder disease and hepatitis. These, except, strangely, gall-bladder disease, greatly increase the mortality. The patients were followed up as far as possible, some for twenty-three years, and during this time 31 died.

The results of treatment are shown to depend more on the severity of the disease than on the treatment itself. However, cholecystostomy in the presence of gall-bladder disease had a very high mortality rate.

The ætiology is discussed, but no further light is thrown on the subject except perhaps for some relevant negatives.

Acknowledgements.

I wish to thank Dr. Wallace Freeborn, the general medical superintendent of the Royal North Shore Hospital, for permission to examine the relevant records and to publish the material in this paper. I wish also to thank Miss D. Drake, of the Unit of Clinical Investigation, for her help in the follow-up of these patients and in the preparation of this paper. I am indebted to Miss A. Scougall, librarian to the Royal North Shore Hospital, for her help in preparing the relevant literature.

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VENOUS OCCLUSION PLETHYSMOGRAPHY: II. AN AID TO THE DIAGNOSIS AND MANAGEMENT OF PERIPHERAL VASCULAR DISEASE.

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In a previous paper (Barnett, 1950) the procedure of venous occlusion plethysmography was critically discussed and a technique involving use of an air-filled plethysmograph was described. It was concluded that, although it was not a method of high accuracy, plethysmography was capable of giving valuable information concerning the blood flow if certain errors in the apparatus and method were avoided. The present paper illustrates the use of the procedure in clinical medicine.

It has been suggested that although a reasonably accurate estimate of the peripheral blood flow may be made by venous occlusion plethysmography in normal persons, this is not so in persons with arterial disease. In the

latter, the blood supply may occur through small, superficially situated collateral vessels in which the pressure is so low that there is a possibility that the venous occlusion pressure may also obstruct the arterial inflow and thus make the recorded blood flow an under-estimate (Grant and Pearson, 1938). This, however, will not invalidate the method as a diagnostic procedure for the presence or absence of arterial occlusion; but it is possible that some of the estimates of blood flow obtained in cases of peripheral arterial occlusion reported in this communication are unduly low.

In view of this objection it becomes important to determine (*a*) the pressure in the collateral vessels in cases of obstruction of the main vessel, and (*b*) the least pressure which will cause satisfactory venous occlusion.

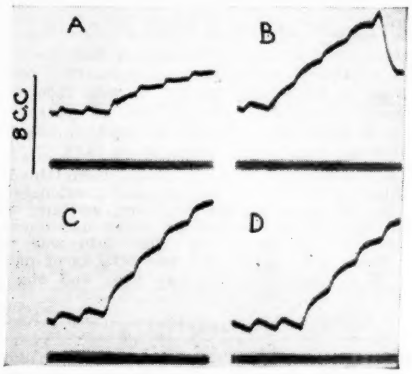

FIGURE I.

Foot plethysmograms from normal subject. A: resting. B, C, D: after reactive hyperæmia test. The recordings were taken one-quarter and three-quarters of a minute and two minutes after release of arterial occlusion. Vertical line: standardization (displacement of tracing by injection of eight millilitres of fluid into plethysmograph). Time markings in tenth of a second. Standardization: 1·0 millilitre = 3·7 millimetres' rise. In this subject the resting blood flow was 1·8 millilitres per 100 millilitres per minute, and maximum blood flow after the reactive hyperæmia test 8·8 millilitres per 100 millilitres per minute (recorded one-quarter of a minute after release of arterial occlusion).

In respect of the pressures in vessels distal to a block, some recent observations of Winsor (1950) are of interest. This author, using a plethysmographic method, found that although the systolic pressure was considerably reduced below the block, it remained above 40 millimetres of mercury. According to the observations of Landowne and Katz (1942), the blood flow is not decreased until the venous occlusion pressure approaches the systolic arterial blood pressure. These workers stated that the lowest level of venous occlusion pressure necessary to ensure collapse of the veins and produce a steady level of the recorded blood flow was 50 millimetres of mercury. However, the present writer has found that on occasions the venous occlusion cuff pressure could be as low as 20 millimetres of mercury without appreciable falling off of the recorded blood flow. It is concluded, therefore, that if a venous occlusion pressure of 40 to 50 millimetres of mercury is used, there will probably not be a great error in the estimation of the blood flow in most cases. However, this question needs more thorough investigation.

Normal Plethysmographic Findings and Changes in Peripheral Vascular Disease.

Pulse Waves.

The normal plethysmogram shows clear pulse waves (Figure I). In tracings from limbs the subject of occlusive vascular disease these are diminished or absent (Figure IIIB).

Resting Blood Flow.

The resting blood flow is subject to pronounced individual variation. However, that recorded in most normal subjects falls within the range of 0·5 to 1·5 millilitres per 100 millilitres per minute (Figure II). In limbs the subject of peripheral arterial disease the resting blood flow may be normal or decreased. In subjects with spasm of small vessels it is decreased; in subjects with organic occlusion of the large vessels it is often normal.

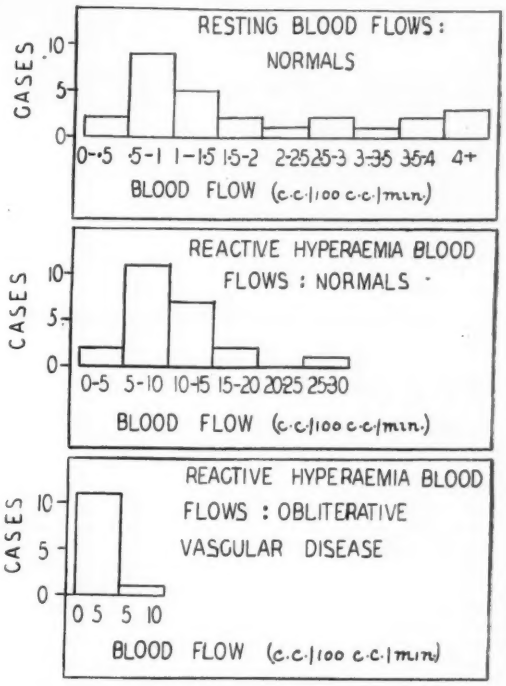

FIGURE II.

Blood flow records from feet of normal subjects and from patients with obliterative arterial disease diagnosed on clinical grounds.

Blood Flow in Response to a Reactive Hyperæmia Test.

In normal persons a reactive hyperæmia test performed by the production of circulatory arrest for ten minutes is followed by a pronounced increase in the blood flow. Although there is considerable individual variation in normal subjects (Figure II), the maximum blood flow recorded after this test is usually within the range of 5·0 to 15 millilitres per 100 millilitres per minute. In cases of vascular disturbance due to spasm (as in Raynaud's phenomenon), the maximum blood flow following the reactive hyperæmia test is normal. In cases of organic arterial disease (as in *atherosclerosis obliterans* and Buerger's disease), it is usually below 5·0 millilitres per 100 millilitres per minute (Figure II).

The blood flows recorded by the writer may be compared with those of Landowne and Katz (1942), who used a somewhat comparable technique (air-filled plethysmograph and arterial occlusive reactive hyperæmia test). They found the resting blood flow to range from 0·5 to 6·0 millilitres per 100 millilitres per minute and the maximum flow following release of arterial occlusion to be 6·3 to 22·5 millilitres per 100 millilitres per minute. These values are rather higher than the writer's, but this may be due to the fact that their plethysmograph enclosed about a third of the lower part of the leg as well as the foot.

Time of Occurrence of the Maximum Blood Flow following the Reactive Hyperæmia Test.

In normal persons the maximum blood flow following the release of the arterial occlusion occurs early (within the first minute). (See Figure I.) In cases of occlusion of a large artery it is late (after one minute). (See Figure IIIB.) The writer has observed this change sufficiently frequently to regard it as an important diagnostic feature. The phenomenon has been previously noted and discussed by Landowne (1942), although he was unable to explain it. It would seem to the writer that the most likely mechanism is as follows. During the period of arterial occlusion there is in the limb distal to the

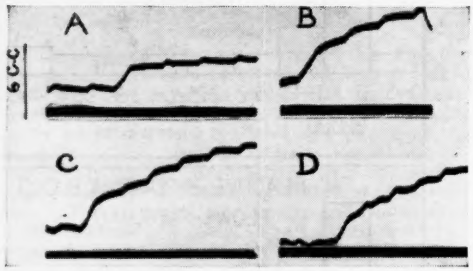

FIGURE IIIA.

Plethysmograms from W.B., right foot. A: resting. B, C, D: after reactive hyperæmia test (recordings one-quarter, one-half and three-quarter minutes after release of arterial occlusion). Standardization: 1·0 millilitre = 3·7 millimetres' rise.

occluding cuff a redistribution of blood from the arteries to the veins and capillaries until the intravascular pressures are equalized. As a result the arteries are less than normally filled. This will occur both in the limb with normal vessels and in that with diseased vessels. In the limb with normal vessels, within a few seconds of the release of the arterial occlusion cuff the arteries are again normally filled. In the limb with obstruction of the large vessels blood has to leak slowly past the obstruction (either through the narrowed lumen or by collaterals), and it may take a minute or more before they are filled sufficiently to produce the necessary pressure to cause the maximal blood flow.

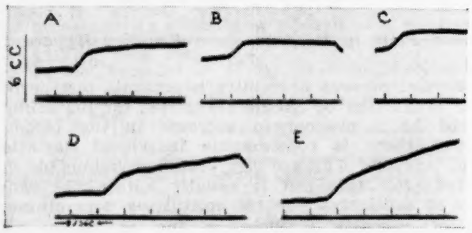

FIGURE IIIB.

Plethysmograms from W.B., left foot. A: resting. B, C, D, E: after reactive hyperæmia test (recordings one-half and three-quarters of a minute and one and one-quarter and one and one-half minutes after release of arterial occlusion). Standardization: 1·0 millilitre = 4·3 millimetres' rise.

Reports of Cases Illustrating the Value of Venous Occlusion Plethysmography in Diagnosis.

Organic Arterial Occlusion.

The characteristic plethysmographic findings in patients with obliterative vascular disease have been described in the previous section. The findings in the following case are fairly typical.

W.B., a man, aged sixty-four years, complained that for the past five months on walking 300 to 400 yards on the flat he had experienced in the outer aspect of his left leg pain severe enough to cause him to stop. The pain then disappeared in five to ten minutes, after which he could walk again a similar distance before experiencing it once more. On examination he was found to be hypertensive; his systolic blood pressure was 220 millimetres of mercury and his diastolic pressure 120 millimetres. Both feet were blue and cold. Pulsation was felt in both popliteal arteries and in the right *dorsalis pedis* and posterior tibial arteries, but not in the left *dorsalis pedis* and posterior tibial arteries. An exercise test over standard steps produced typical claudication pain in the left anterior tibial region. A radiogram of the lower limbs showed partial calcification of the femoral vessels, but no calcification in the tibial vessels. Plethysmography gave the following results. (See Figures IIIA and IIIB.)

The findings were held to confirm the presence of obliterative arterial disease of the left lower limb.

Vascular Disturbance due to Spasm.

Although a certain element of spasm may be associated with organic arterial occlusion, and spasmodic contraction of vessels as in Raynaud's disease is well recognized, the occurrence of functional contraction of vessels of the lower limb of sufficient intensity to produce ulceration as in the following case would seem to be rare.

R.J., a spinster, aged forty-six years, complained that at the beginning of the winter six months previously she had suffered gradual onset of discoloration, swelling and pain of her left leg. More recently an ulcer had developed on the ball of her left great toe. The pain was worse on walking. There were no paroxysmal attacks of pallor or of cyanosis. Her general health was poor and she "had no

TABLE I.

State of Patient.	Blood Flow. (Millilitres per 100 Millilitres per Minute.)	
	Right Foot.	Left Foot.
Resting	0·8	0·6
After reactive hyperæmia test ..	5·4	3·5

energy", but there were no other specific complaints. Her menses were becoming less frequent and more scanty in recent months. Her weight was always between six stone three pounds (39·5 kilograms) and six stone six pounds (40·9 kilograms).

Examination revealed the patient to be very thin. Her blood pressure was 150 millimetres of mercury, systolic, and 85 millimetres, diastolic. The popliteal, posterior tibial and *dorsalis pedis* arteries pulsated on both sides. Both feet were cold and blanched when elevated. The left foot was blue and there was an ulcer on the ball of the left great toe.

By plethysmography the resting blood flow from the left foot was found to be 0·6 millilitre per 100 millilitres per minute. The intramuscular injection of 25 milligrammes of pentamethonium iodide produced no significant change in the blood flow in the left foot, in the skin temperature of the right foot, or in the blood pressure. After a reactive hyperæmia test a blood flow of 10 millilitres per 100 millilitres per minute was recorded from the left foot. The lack of response from the injection of the pentamethonium iodide was puzzling, particularly as the writer had previously found it efficacious in relieving vascular spasm. Further investigation was carried out two weeks later. On this occasion the resting blood flow from the left foot was found to be one millilitre per 100 millilitres per minute, and the blood flow after the reactive hyperæmia test 8·5 millilitres per 100 millilitres per minute. After a lapse of some twenty-five minutes to allow the increase in blood flow from reactive hyperæmia to subside (to 1·5 millilitres per 100 millilitres per minute), 50 milligrammes of pentamethonium iodide were given by intramuscular injection, and this was followed twenty-two minutes after the injection by a rise in the blood flow to 3·8 millilitres per 100 millilitres per minute. There occurred also a slight fall in the brachial blood pressure and a rise in the skin temperature of the right foot (Figure IV). Plethysmograms are shown in Figure V. The lack of response to the injection of 25 milligrammes and good response to that of 50 milligrammes of pentamethonium iodide are difficult to explain. It would seem that a certain

minimum amount of the drug was necessary to abolish the sympathetic nervous overactivity producing the spasm. As a result of these investigations it was possible to exclude the presence of organic arterial occlusion and to predict that blocking of the sympathetic nervous supply to the lower limbs (either by sympathectomy or by the administration of a ganglionic blocking agent) should alleviate the patient's symptoms. Sympathectomy has since been performed with considerable benefit.

Absence of Occlusive Vascular Disease.

The following cases illustrate the value of plethysmography in excluding the presence of occlusive arterial disease as a cause of symptoms.

J.B., a man, aged twenty-five years, was referred for plethysmography on February 2, 1950. He gave a history of a motor-cycle accident in 1941, when he had sustained a fracture of his left femur and dislocation of his left hip. He had been in and out of hospital many times and had had various operations including an arthrodesis of his left hip.

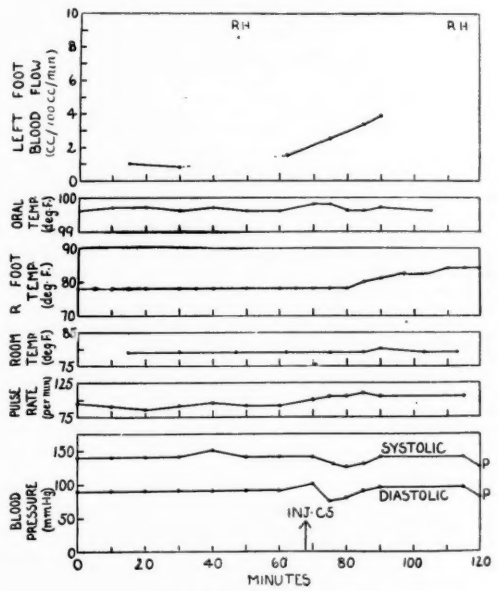

FIGURE IV.

Chart of findings in investigation of R.J. R.H., reactive hyperæmia. P., blood pressure readings when the patient had assumed the sitting posture. At arrow 50 milligrammes of pentamethonium iodide were injected intramuscularly.

About the middle of 1947 his left foot began to swell and became discoloured, and shallow ulcers appeared on the dorsal aspect of his toes. Because of this complaint a left lumbar sympathectomy was performed in November, 1948. There was some improvement after this operation; but within a month of the patient's returning to his work his condition was almost as bad as before. Because of the pain in his foot, the left musculo-cutaneous and left sural nerves were crushed (December, 1949, and January, 1950). On examination in February, 1950, the patient was found to be a plump, miserable young man. His blood pressure was 120 millimetres of mercury, systolic, and 80 millimetres, diastolic. The left foot was swollen with shallow ulceration of the dorsum. Arterial pulses were normally palpable in both lower limbs, being stronger in the left (affected) foot than in the right. Plethysmography on February 2, 1950 (Figure VI), showed the resting blood flow in the left foot to be 2·4 millilitres per 100 millilitres per minute, and the blood flow after a reactive hyperæmia test 11·2 millilitres per 100 millilitres per minute (these values being higher than on the unaffected side). These results were interpreted as excluding occlusive vascular disease as the cause of the symptoms. However, because of the pain, a below-the-knee amputation of the leg was performed some three weeks later. The wound healed, but soon after his discharge from hospital he fell onto the stump which has been persistently ulcerated since. He was still in hospital in March, 1951, and although the ulceration had healed he had pain in the stump similar to that previously experienced in the foot.

In another young man referred recently because of a chronic ulcer of the foot following a war injury it was possible to demonstrate a high normal resting blood flow with good response to reactive hyperæmia. The ulceration was regarded as being of "trophic" origin due to nerve injury, and the patient was saved sympathectomy, the results of which would probably have been disappointing as in the case of J.B.

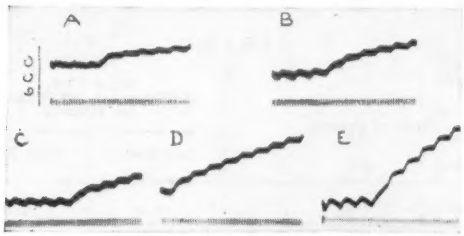

FIGURE V.

Plethysmograms from R.J., left foot. A: resting. B, C, D: 13, 23 and 28 minutes after intramuscular injection of 50 milligrammes of pentamethonium iodide. E: after reactive hyperæmia test. Standardization: 1·0 millilitre = 4·2 millimetres' rise.

A middle-aged woman of Continental origin had become convinced that she suffered from occlusive vascular disease because of pain down the front of her leg on walking. Although the history was not typical of intermittent claudication of vascular origin, and the pain was probably neuritic in nature (possibly from involvement of a nerve in a scar higher in her leg), the demonstration by plethysmography of normal blood flows helped to rid her mind of the fear of a dread disease.

Investigation of the Action of Vaso-active Drugs.

Nicotinic Acid.

After an intramuscular injection of 50 milligrammes of nicotinic acid, which has a wide reputation as a vasodilator, there is observed flushing of the face and usually of the hands, and sometimes of the upper part of the

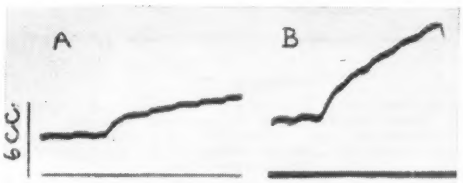

FIGURE VI.

Plethysmograms from J.B., left foot. A: resting. B: after reactive hyperæmia test. Standardization: 1·0 millilitre = 3·8 millimetres' rise.

trunk; but the writer has never observed flushing of the legs or feet. It was therefore of interest to determine whether this substance might be of value in treatment of conditions with diminished blood flow to the lower limbs. The administration of nicotinic acid in a dosage of 100 milligrammes given orally or 50 milligrammes given by intramuscular injection to 12 subjects (only one of whom had definite peripheral disease) was followed by an increase in blood flow in eight, a decrease in one and no change in three (Table III). This series is too small for any firm conclusions to be drawn; but the results suggest that nicotinic acid is an inconstant vasodilator agent in the lower limbs.

"Priscol."

The following case summaries show the value of plethysmography in demonstrating whether or not "Priscol" (2-benzyl-imidazoline hydrochloride) will cause an increase in blood flow in a particular patient.

R.P., aged seventy-four years, complained that on walking he experienced pain in his left calf, which caused him to stop. The pain would then go away in a few minutes. (He also suffered from prostatic symptoms, hernia and osteo-arthritic pain of the right knee.) His blood pressure was 145 millimetres of mercury, systolic, and 60 millimetres, diastolic. The radial arteries were grossly thickened. However, the *dorsalis pedis* and posterior tibial pulsations were palpable on both sides. The feet were cold and there were small areas of skin necrosis. Plethysmography revealed a

TABLE II.

State of Patient.	Blood Flow. (Millilitres per 100 Millilitres per Minute.)	
	Left Foot.	Right Foot.
Resting	5·0[1]	1·7
Two minutes after intravenous administration of 20 milligrammes of "Priscol".	Not recorded.	1·0
After reactive hyperæmia test ..	7·2	Not recorded.

[1] The high resting blood flow from the left foot is probably due to the presence of acute gout.

resting blood flow from each foot of 0·5 millilitre per 100 millilitres per minute, with a maximum after the reactive hyperæmia test of 4·7 millilitres per 100 millilitres per minute. He was treated with Buerger's exercises and anti-coagulants, and twelve days later the areas of skin necrosis had disappeared. Plethysmography (Figure VII) showed a resting blood flow of 0·5 millilitre per 100 millilitres per minute, with an increase to 1·4 millilitres per 100 millilitres per minute three minutes after the intravenous injection of 20 milligrammes of "Priscol", and a further increase to 9·0 millilitres per 100 millilitres per minute after the reactive hyperæmia test. It is suggested that in this case there was thrombosis in small vessels associated with spasm.

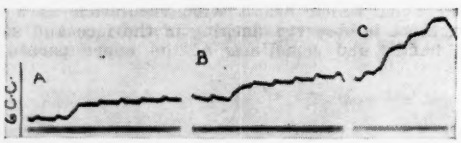

FIGURE VII.

Plethysmograms from R.P., left foot. A: resting. B: three minutes after intravenous injection of 20 milligrammes of "Priscol". C: after reactive hyperæmia test. Standardization: 1·0 millilitre = 5·0 millimetres' rise.

In the following case no increase in blood flow followed the injection of "Priscol".

F.P., aged eighty-five years, stated that fifteen months earlier he had developed pain in his right foot. Operation (lumbar sympathectomy) had been performed three months later, since when he had had pain in both calves on walking 100 yards, causing him to stop, after which the pain went away in three or four minutes. Also he experienced rest pain in his left leg when in bed at night.

On examination of the patient, both feet were blue and cold and paled on elevation. Pulsation was palpable in the popliteal arteries, but was feeble in the posterior tibial arteries and absent in the *dorsalis pedis* arteries. Plethysmography (Figure VIII) showed a resting blood flow of 1·0 millilitre per 100 millilitres per minute, with no increase following the intramuscular injection of 20 milligrammes of "Priscol", but a rise to 2·0 millilitres per 100 millilitres per minute after the reactive hyperæmia test (recorded two and a half minutes after the release of the arterial occlusion).

In one case the injection of "Priscol" was followed by a decrease in the blood flow of a limb subject to occlusive vascular disease.

E.R.W., aged fifty-five years, had suffered from intermittent claudication in his right leg for four years. Two weeks prior to investigation he had had an attack of podagra in his left great toe and one week later he had a similar attack in his right great toe. Plethysmography gave the results shown in Table II. (See Figure IX.)

The reduction in blood flow in the affected leg following the injection of "Priscol" can probably be explained by vaso-dilatation in other areas and diversion of blood to them at the expense of the affected limb, in which the blood flow could not be further increased because of the organic occlusion.

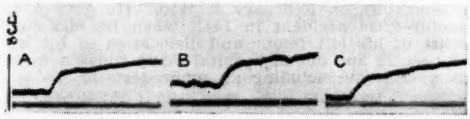

FIGURE VIII.

Plethysmograms from F.P., left foot. A: resting. B: eighteen minutes after intramuscular injection of 20 milligrammes of "Priscol". C: after reactive hyperæmia test (recording taken two and a half minutes after release of arterial occlusion). Standardization: 1·0 millilitre = 3·0 millimetres' rise.

Methonium Compounds.

The vasodilator effect of pentamethonium iodide in a patient with a vasospastic condition of the lower limbs has been illustrated in the case of R.J. Also in the following case of organic occlusion, the administration of this substance was effective in increasing the blood flow.

R.D.McC., aged sixty-four years, complained of pain in the right leg on walking during the last two years, and of pain in the left leg for the last two months, if he tried to "walk through" the pain in the right leg.

On examination of the patient, the blood pressure was 160 millimetres of mercury, systolic, and 88 millimetres, diastolic. Both feet were cold and blue. Both femoral arteries pulsated normally, but no pulsation was felt in the popliteal or foot arteries. However, oscillometry revealed moderate pulsation in both calves. Exercise over standard steps produced claudication pain.

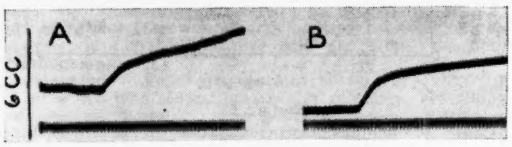

FIGURE IX.

Plethysmograms from E.R.W., right foot. A: resting. B: two minutes after intravenous injection of 20 milligrammes of "Priscol". Standardization: 1·0 millilitre = 5·3 millimetres' rise.

Plethysmography gave the following results (Figure X). The resting blood flow from the left foot was too low to record; twenty minutes after the intramuscular injection of 50 milligrammes of pentamethonium iodide ("Antilusin"—Allen and Hanbury) it had risen to 1·5 millilitres per minute. The maximum blood flow recorded after the reactive hyperæmia test was 1·9 millilitres per 100 millilitres per minute (three minutes after release of the arterial occlusion).

As a result of the improvement in blood flow from the use of a sympatholytic drug, it was predicted that lumbar sympathectomy would be of value. This operation was performed, and the toes became warm and pink and pulsation became palpable in both *dorsalis pedis* and posterior tibial arteries. The claudication was not affected.

In the following case the administration of pentamethonium iodide was ineffective in producing an increase in blood flow on the affected side.

F.G., aged sixty-nine years, complained that over the last six months he had experienced aching in the legs, mainly

TABLE III.
Effect of Nicotinic Acid on Foot Blood Flow.[1]

Subject.	Age. (Years.)	Sex.	Clinical Condition.	Blood Flow. (Millilitres per 100 Millilitres per Minute.)				Comment.
				Before Administration of Nicotinic Acid.	After Oral Administration of Nicotinic Acid (100 Milligrammes).	After Intramuscular Injection of Nicotinic Acid (50 Milligrammes).	Maximum After Reactive Hyperæmia Test.	
H.M. ..	59	M.	Functional hyperidrosis.	0·5	2·5	4·1	12·1	Increase.
J.D. ..	32	F.	Essential hypertension.	1·75	7·0	—	22·0	Increase.
J.B. ..	25	M.	Pain and ulceration in left foot following injury to left hip and femur.	5·6	2·0	—	5·0	Fall.[3]
F.C. ..	58	F.	Diabetes.	3·4	—	3·6	—	No change.
W.P. ..	30	M.	Bronchospasm.	2·3	—	3·9	10·9	Increase.
M.P. ..	44	F.	After sympathectomy for Raynaud's disease.	1·4	—	1·3	16·0	No change.
W.A. ..	61	M.	After pneumonia; cold feet and hands.	0·6	—	0·7	9·2	No change.
C.S. ..	59	M.	Atherosclerosis; intermittent claudication.	0·3	—	1·1	4·0	Increase.
F.S. ..	25	M.	Spontaneous pneumothorax.	0	—	0·8	7·0	Increase.
McG. ..	53	F.	Rheumatic heart disease (aortic incompetence and mitral stenosis).	3	—	5·5	11·8	Increase.
A.M.J.[2]	62	F.	Essential hypertension.	5·7	—	7·9	9·2	Increase.
L.N. ..	42	M.	Ulcerative colitis.	0·8	—	1·2	15·0	Increase.

[1] Oral temperature, pulse rate, and blood pressures were recorded before and after administration of nicotinic acid. They showed no consistent changes and for the sake of simplicity have not been included in the table.

[2] The resting blood flow in this case was approximately equal to that obtained at another examination of the same patient after the reactive hyperæmia test, suggesting that full vasodilatation was already present in the foot before the administration of nicotinic acid. The records tabulated were made from the right foot.

[3] This patient complained of pain in the calves on walking, but the clinical findings and blood flow do not support a diagnosis of obliterative vascular disease.

in the right calf and thigh, on walking, with ease within a few minutes of stopping. On examination of the patient, the blood pressure was 140 millimetres of mercury, systolic, and 60 millimetres, diastolic. Pulsation was present in all arteries of the legs, but was less pronounced on the right side from the femoral artery down.

By plethysmography the resting blood flow in the left foot was found to be 1·1 millilitres per 100 millilitres per minute, with a rise to 8·3 millilitres per 100 millilitres per minute following the reactive hyperæmia test. In the right foot (Figure XI) the resting blood flow was 2·0 millilitres per 100 millilitres per minute, rising to 4·8 millilitres per 100 millilitres per minute as a result of the reactive hyperæmia test. When the right foot blood flow had fallen to 3·0 millilitres per 100 millilitres per minute an intramuscular injection of 50 milligrammes of pentamethonium iodide was given. This failed to produce any increase in the right foot blood flow, and a reactive hyperæmia test did not result in the increase obtained by its application prior to the injection of the drug.

After the injection of the pentamethonium iodide, there was a pronounced fall in blood pressure and a pronounced increase in the skin temperature in the left foot. The lack of response to the reactive hyperæmia test in the affected lower limb could possibly be explained by the diversion of blood to the regions more capable of vasodilatation and the associated fall in blood pressure.

Discussion.

Three main requirements of any diagnostic measure are that it should be reasonably safe, that it should be sufficiently accurate, and that it should give information not readily obtainable in some simpler way.

At this hospital no untoward accidents have been experienced as a result of plethysmography, nor has any reference to these by other workers been noted. The application of an arterial occlusion cuff causes minor discomfort, but has had no ill effects. As it is theoretically possible that the pressure may break up a recent thrombus and thus give rise to emboli to smaller vessels, the test has never been carried out on any patient with a history suggesting a thrombotic lesion of the limb within the previous three weeks. It would seem to the writer that the arterial occlusion reactive hyperæmia test is safer than certain others which employ the local application of heat.

With regard to accuracy, venous occlusion plethysmography cannot be looked upon as a precise method of absolute measurement. In normal persons the recorded blood flow is probably correct only to the nearest 0·25 millilitre. In patients with obliterative vascular disease, as has already been pointed out, the recorded blood flow may be an under-estimate. With regard to accuracy in diagnosis by the avoidance of "false positive" and "false negative" results, it is considered that the test compares favourably with most other laboratory procedures. The range of normal both of the resting blood flow and of that following the reactive hyperæmia test (the more useful value in diagnosis) is very large. However, practically all the normal subjects have had a maximal

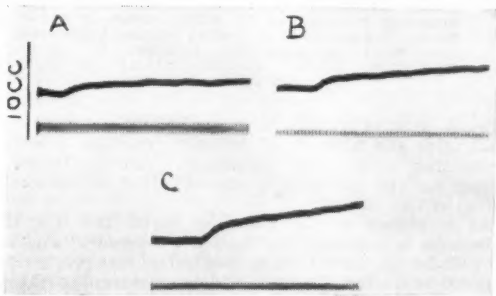

FIGURE X.

Plethysmograms from R.D.McC., right foot. A: resting. B: twenty minutes after intramuscular injection of 50 milligrammes of pentamethonium iodide. C: after reactive hyperæmia test (recording three minutes after release of arterial occlusion). Standardization: 1·0 millilitre = 2·7 millimetres' rise.

blood flow following the reactive hyperæmia test of over 5·0 millilitres per 100 millilitres per minute, and practically all the subjects with peripheral vascular disease have a maximal blood flow below this level (Figure II). In doubtful cases other features of help are the following: presence and size of pulse waves, time after arterial release for the occurrence of the maximal degree of hyperæmia, comparison with blood flow from the other side.

In respect to the supply of information not readily obtainable in some simpler way, venous occlusion plethysmography scores most highly. It is the only simple pro-

cedure which gives a quantitative measure of blood flow. Other measures, such as determination of rate of flow through the main artery or rate of removal of radioactive materials injected into tissues, are not suitable for routine clinical use. The forms of microplethysmography (of finger or toe) which do not also use venous occlusion record only pulse volume changes and not blood flow. Skin temperature changes are subject to so many influences that they are not of great value in estimating blood flow. Calorimetry is a valuable method in studying heat elimination which mirrors skin blood flow, but cannot record the total blood flow through a part. It is not easily adapted to the foot.

In cases of organic arterial occlusion plethysmography is not necessary for the diagnosis, which can usually be made readily by clinical means, aided perhaps by oscillometry. However, even here the method has value by giving a quantitative estimate of the blood flow and determining what response is possible from vasodilator procedures. In cases of disturbance of circulation due to spasm the diagnosis could be established by other means—changes in the appearance and temperature of the skin after "reflex" hyperæmia from heating other parts—but not in the quantitative manner of venous occlusion plethysmography. Probably one of the greatest

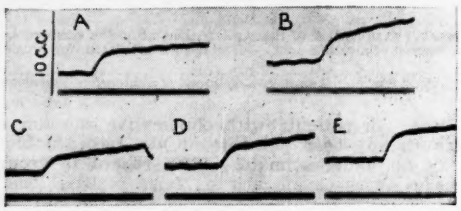

FIGURE XI.

Plethysmograms, F.G., right foot. A: resting. B: after reactive hyperæmia test (recording one and three-quarter minutes after release of arterial occlusion). C: new "resting" blood flow (increase as result of reactive hyperæmia test has not completely disappeared). D: seven minutes after intramuscular injection of 50 milligrammes of pentamethonium iodide. E: following reactive hyperæmia test after intramuscular injection of pentamethonium iodide. Standardization: 1·0 millilitre = 3·5 millimetres' rise.

clinical uses of venous occlusion plethysmography is in confirming the absence of occlusive vascular disease and preventing unnecessary operation. In the blood flow recordings and plethysmograms objective evidence may be given to the patient.

As is shown by the examples given, the fact that a substance is a vasodilator does not necessarily mean that it will be of benefit in a particular case of peripheral arterial occlusive disease; evidence concerning the latter may be obtained from venous occlusion plethysmography. Also, if the blood flow is improved by the use of a sympatholytic drug, this is an indication that surgical sympathectomy will also be of benefit. (However, the converse is not necessarily true. If the blood flow is not increased by a sympatholytic drug it is still possible that lumbar sympathectomy of the affected side may be of value, as in the latter case there is no widespread vasodilatation or fall in blood pressure.)

It is concluded that, if used with appreciation of its limitations, venous occlusion plethysmography is a valuable aid in the diagnosis and management of peripheral vascular disease.

Summary.

1. Venous occlusion plethysmography of the foot has been used as a diagnostic measure in cases of peripheral arterial diseases.

2. Normal blood flow and plethysmograms from the foot and the changes in these in peripheral arterial disease are described.

3. Illustrative case histories are given showing the value of venous occlusion plethysmography in the diagnosis of organic arterial occlusion, vascular disturbance due to spasm, and absence of occlusive vascular disease.

4. The value of venous occlusion plethysmography in the investigation of the action of peripheral vasodilator drugs is illustrated by reference to a study of the action of nicotinic acid, and a description of the effects of "Priscol" and pentamethonium iodide in individual patients.

5. It is held that, although it has limitations which should be recognized, venous occlusion plethysmography reasonably fulfils the requirements of a diagnostic test and may give valuable aid in the diagnosis and management of peripheral vascular disease.

Acknowledgements.

Grateful acknowledgement is made to Dr. T. E. Lowe, Director of the Baker Medical Research Institute, and of the Clinical Research Unit at the Alfred Hospital, for encouragement and much helpful advice; to members of the laboratory staff for assistance in making examinations; and to honorary physicians and surgeons of the Alfred Hospital for referring patients for investigation.

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THE PROBLEM OF SIMPLE GOITRE.[2]

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IT is fortunate that iodine, the raw material of thyroxine, is so readily absorbed into the human body. In fact, the ease of absorption of iodine is remarkable. Even painting iodine on the skin, or taking a bath in water containing iodine, causes a measurable rise in the blood iodine level (Fellenberg, 1930). So the age-old custom of painting iodine on the neck in simple goitre was not without benefit, though of course the iodine could equally well have been painted on the leg or forearm.

It is also known that our iodine intake determines the weight of our thyreoid gland. Thus, the average weight of the thyreoid from normal subjects in England and Wales, and probably in coastal Australia too, is about 25 grammes. But if the diet is very rich in iodine the gland will be undersized by this standard. For example, in Iceland, where the inhabitants largely subsist on fish, the average thyreoid weight in adults is only about 12 grammes —or less than half the weight in the United Kingdom.

On the other hand, towards the centre of continents the thyreoid enlarges (Thomas, 1934). In general, the further

[1] Additional references are to be found at the foot of the first article of this series (Barnett, A. J., *loco citato*).

[2] Read at a combined meeting of the City of Newcastle Medical Advisory Committee and the Central Northern Medical Association, at Newcastle, New South Wales.

we go from the sea, the lower the iodine intake and the larger the thyreoid. If the iodine intake is low the gland may so increase in size that it becomes goitrous.

When is thyreoid enlargement classified as goitrous? We define a goitre as any visible or palpable enlargement of the thyreoid gland. Of course, such criteria are quite rough. Thus if the neck is thin the thyreoid may be palpable, even though it is not greatly enlarged. But thyreoid enlargement is significant if it is well marked and if the goitre is firm, asymmetrical or nodular.

Figure I shows the stages in iodide uptake, hormone synthesis and hormone secretion. All these take place in the cells of the thyreoid. In whatever form it is taken by mouth, iodine is finally presented to the gland solely as the iodide; it is then converted by an intracellular oxidase into elemental iodine, which is combined to form diiodotyrosine. By the oxidative coupling of two molecules of diiodotyrosine we get our thyroxine, which is stored in the follicle as thyreoid protein (thyroglobulin) and used as required.

Clearly, the first requirement in the elaboration of thyroxine is iodine itself, and if the blood iodide content is inadequate the output of thyroxine tends to fall. This fall in the thyroxine content of the blood and tissue fluids is felt especially by the cells of the anterior lobe of the pituitary.

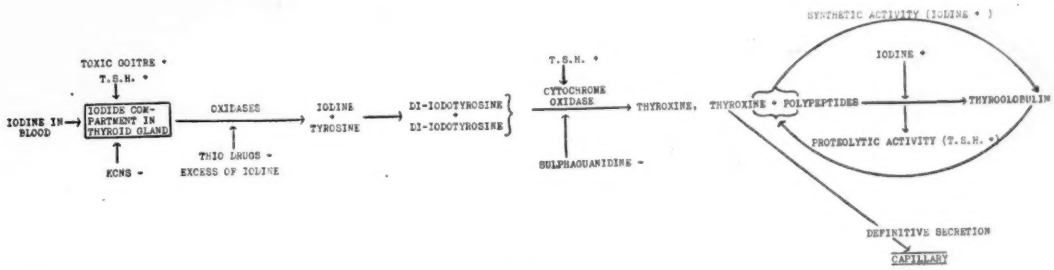

FIGURE I.
Hormone synthesis.

There is good evidence, which need not be detailed here, to show that the anterior lobe of the pituitary is very sensitive to the blood thyroxine level. When this blood thyroxine level falls, the anterior pituitary lobe secretes a thyreoid-stimulating hormone (T.S.H.) which activates the thyreoid, causing it to undergo hyperplasia.

To summarize, then, the essential mechanism of simple goitre is iodine deficiency, a tendency for the thyroxine output of the gland to fall, an increased secretion of T.S.H. and finally, compensatory thyreoid hyperplasia.

Such hyperplasia greatly increases the gland's ability to extract iodide from the circulating plasma. Thus, by exposing a greater epithelial surface to the plasma, the hyperplastic gland compensates for the low blood iodide level and the low iodine intake. In fact, if it were not for the goitre these people would all be manufacturing rather too little thyreoid hormone and would be to some degree hypothyreoid. There are, of course, limits to the compensating ability of the thyreoid, and if the iodine intake is very low—as in some endemic areas—there will be clinical evidence of hypothyreoidism along with the goitre.

Before considering the clinical changes with goitre, let us examine the gradient between the serum iodide level and the thyreoid level. This has been studied in detail by Vanderlaan and Vanderlaan (1947). In one of their experiments a group of normal rats was injected with radio-iodine. The thyreoid to serum iodide ratio was then determined and found to be about 30:1. This, of course, merely puts a figure on the known natural avidity of the thyreoid for administered iodine.

In a second group of rats, thiouracil had been administered for two weeks or so and the thyreoids were intensely hyperplastic. After radio-iodine had been given the thyreoid iodide concentration was 250 times that of the serum. The serum to thyreoid iodide gradient was much steeper, or put in another way, epithelial hyperplasia greatly increased the thyreoid's ability to extract iodide from the plasma.

When we turn to the clinical characteristics of iodine-deficiency goitre, it is at once apparent that as well as iodine deficiency there is an individual factor at work. For instance, why in mildly endemic areas is goitre so much more common in females than in males? Again, nearly all the members of one family may be affected, whereas in a nearby family only a few are goitrous, though they have all resided in the area under the same conditions for just as long as the first family.

The incidence of adolescent goitre in a given community is directly proportional to the iodine intake on the one hand and to the frequency of established goitre in the adult population on the other (Murray *et alii*, 1948). Hence, puberty and adolescent goitre are of the greatest significance. They should not be lightly dismissed, but demand prompt and long-continued iodine therapy.

There is, in fact, evidence that the body's demands for thyreoid hormone are increased during periods of active growth and at times of sexual stress or sexual imbalance in the female. So a female whose thyreoid is getting just enough iodine to fulfil her basic requirements may develop hyperplasia at puberty, adolescence, pregnancy or the menopause. Once she is through these epochs the body's demands for thyroxine fall and the gland may involute and again become impalpable. But once the hyperplasia has been very pronounced it is unlikely that the gland will ever revert to normal; it hyperinvolutes and becomes a colloid goitre which later develops nodules. In the nodules every conceivable type of degeneration can occur—hæmorrhagic, fibrous, calcific, and so on.

The foregoing relationships and their general clinical effects are summarized in Table I. Clearly, three variables are involved—namely, the iodine intake, the thyreoid response, and the bodily metabolism. Their possible trends are roughly shown in Figure II. Despite decreasing iodine intake the metabolism and bodily development remain normal over a considerable range because of effective compensation by increase in thyreoid size.

Now what are the basic factors in a low iodine intake? These are as follows: (i) Distance from the ocean: maritime dwellers have ready access to sea foods, all of which are very rich in iodine. (ii) Characters of the soil: the iodine content of the soil determines the iodine content of grasses and so of cow's milk. It also determines the iodine content of all the vegetables and cereals we eat. The iodine content of the soils and rocks also determines the iodine content of our drinking water. The chief factors impoverishing the soil are leeching by percolating waters and alkalinity; for example, lime-rich soils are poor in iodine. Calcium breaks down humus and renders the soil porous and hence easily leeched. Cropping is also important, since substantial quantities of iodine are removed with the harvesting of every crop.

We may now make a quick survey of the world incidence of simple, iodine-deficiency goitre. The magnitude of the problem is little appreciated.

In the United States, goitre is endemic throughout the Appalachian Range, in the States bordering on the Great Lakes (New York, Ohio, Michigan, Indiana and Illinois), through to the Dakotas and into the far west States of Montana, Idaho, Utah, Oregon and Washington. The great central prairies are comparatively free of goitre, as are the States on the Atlantic seaboard. Formerly, a goitre incidence of 40% to 100% was reported among boys and girls in certain localities around the Great Lakes. For years now, iodization of the salt in many of the States has been mandatory and the position has been much improved.

In Central and South America there exists a vast goitre belt extending from the upper basin of the Rio Grande through Mexico and Colombia, along the Cordillera of the Andes through Equador and Peru, as far down as Chile and western Argentina. Surveys in mountain villages show that 80% to 100% of the population are goitrous. In Mexico the problem has been tackled vigorously, and wherever more than 20% are goitrous it is compulsory for any person or firm dealing with salt to iodize it. There are penalties for infringement of this law, ranging from progressive fines to closure of the establishment.

TABLE I.

Effects of Iodine Deficiency.

Iodide Intake and Thyreoid Efficiency.	Clinical Effects.
1. Borderline iodine deficiency or poor thyreoid stock (thyreoid has no "reserve").	Transient thyreoid enlargement at periods of increased demand—puberty, adolescence *et cetera*.
2. Mild or moderate iodine deficiency, or thyreoid inadequate at normal size.	Classical endemic goitre, usually without hypothyreoidism; if of long standing there is much degenerative change in the nodules.
3. Severe iodine deficiency, affecting several generations.	Goitre associated with hypothyreoidism and imperfect physical and mental development. Stunting—dwarfism. Low intelligence quotient—idiocy. Low fertility — repeated miscarriages. Deaf-mutism. Intensely hyperplastic goitre at birth sufficient to cause tracheal pressure. Failure of thyreoid to undergo much hyperplasia, with consequent exhaustion atrophy, leading to infantile or congenital cretinism.

There is a patchy distribution of goitre practically throughout the whole of the African continent, but nowhere is the disease endemic to the same extent as in South America or in the north of India. In Egypt, simple goitre is extremely common among the *fellaheen*, and according to Dolby and Omar, reliefs, statuary and wall paintings prove that goitre was known in the valley of the Nile as far back as 2000 B.C.

The goitre distribution in the United Kingdom has been closely studied, and, as usual, endemics correspond to regions of low iodine content of the food and drinking water. From a recent survey a goitre sub-committee of the Medical Research Council of the Privy Council (1948) has estimated that there are about 500,000 cases of goitre among children and young people aged under twenty-one years, and it has now been decided that all salt retailed for human consumption in the United Kingdom will be iodized (potassium iodide one part to 100,000 parts of salt).

In Norway, Devold and Closs (1941) carried out an interesting survey in the district of Forsand. The goitre incidence was found to increase with the distance from the sea, and it was also demonstrated that the consumption of fish decreased as the distance from the sea increased. In Sweden the prevention of goitre by iodization of the salt has been recommended officially, and appropriate instructions have been circulated to all public health and municipal medical officers.

In Holland, as Reith (1933) has shown, there is a clear inverse relationship between the incidence of goitre and the iodine content of the drinking water. This led to goitre prophylaxis by iodization of the water supply in Holland.

No country has made greater contributions to the story of iodine and goitre than France, where it was Courtois who discovered iodine in 1811, Gay-Lussac who studied and named it in 1813, and Boussingault who first advised iodized salt for goitre prevention in 1831. In the eastern zone the heaviest endemics are in the Savoy, but in the High Pyrenees to the south-west there are still some of the most notorious endemics in Europe, with frequent cretinism and deaf-mutism.

The most important focus of goitre in Spain and one of the best known in Europe is in the area of Las Hurdes, about 150 miles west of Madrid. In its rough and inhospitable valleys, goitre, cretinism, deaf-mutism, dwarfism and idiocy abound. Not a single man from the district has ever been found fit for military service because of the prevailing low stature and feeble-mindedness.

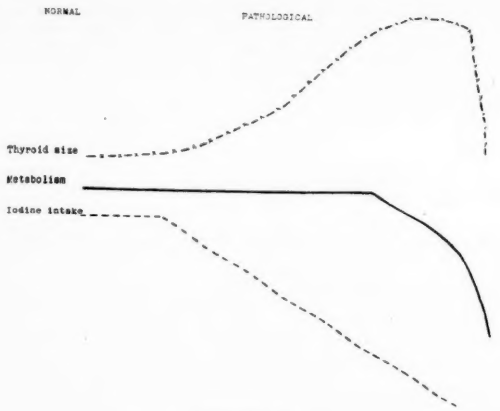

FIGURE II.

Theoretical concept of concomitant changes in thyreoid size, and in bodily development and metabolism, with decreasing iodine intake. When iodine deficiency is severe, compensation fails and there occur ultimately thyreoid aplasia and cretinism.

In Switzerland and the Alps endemic goitre is, of course, a serious menace to the public health, and as is well known, no part of the country is free from the disease. Prior to the introduction of iodized salt in 1924, the percentage of goitre among Swiss army recruits ranged up to 63% in the north-eastern Cantons. But since 1924 the incidence has decreased sharply.

In Italy there are interesting references to goitre in the classical literature. Thus the Roman architect Vitruvius (*circa* 63 B.C. to A.D. 14) wrote that "the drinking water of the Italian Alps is of such a nature that all using it are afflicted with swelling of the throat". Likewise Pliny the Elder (*circa* A.D. 23 to 79) ascribed the cervical swelling common in the Po valley to the deleterious quality of the drinking water.

All through the Black Forest and Bavaria goitre abounds, and Aschoff reported from Freiberg (1935) that out of 448 stillbirths and neo-natal deaths about 90% were probably due to pressure on the trachea by an enlarged thyreoid. In the mountain districts of eastern Moravia, too, 80% to 90% of the villagers are goitrous, and a high proportion are also hypothyreoid.

Further east we come to Bulgaria, where in the hills just south of Sofia there arises the river Struma, which

flows southward through Greece to the Ægean. Its name is famous because it became applied to the cervical swelling which abounds among the inhabitants of its valleys. In Rumania, the severest endemics occur in the Carpathian Mountains. Dwarfism, mental retardation and cretinism are common (Danielopolu, 1937).

However, the most notorious goitre belt in the world is that extending almost continuously for more than 1500 miles along the southern slopes of the Himalayas in the north of India. Over wide areas the entire population is goitrous, and in the United Provinces alone 100,000 persons are treated annually for goitre. The goitres are very often huge and cause difficulty in breathing and swallowing; Stott and Gupta (1933-1934) described one patient who took two hours to eat a meal. Distended veins are often prominent over the surface of the goitre, and congestion of the face and legs is frequent.

I may digress to say that the best modern surgery, with its remarkable safety and negligible morbidity, has solved the problem of such cases. In fact, surgical intervention is advisable whenever the goitre, by virtue of either its size or its location, causes symptoms of pressure on the trachea or adjacent structures. Malignant and certain other degenerative changes also indicate surgical treatment. At the same time, it should be emphasized that there is no need to advise surgical treatment for the patient who has had a small diffuse or multinodular goitre for many years without symptoms. In endemics the world over such patients live happy and useful lives.

Table II.

Country.	Parts of Iodide in Parts of Salt.	Added as.
United States of America.	1 in 10,000	Potassium iodide.
Canada	1 in 10,000	Sodium iodide or potassium iodide.
New Zealand ..	1 in 20,000	Sodium iodide or potassium iodide.
United Kingdom ..	1 in 100,000	Potassium iodide.
Switzerland ..	1 in 100,000	Sodium iodide or potassium iodide.
Holland	1 in 100,000	Potassium iodide.
Italy	1 in 100,000	Potassium iodide.
Poland	1 in 200,000	Potassium iodide.
Germany	1 in 200,000	Potassium iodide.

We may skip over the endemics of the Caucasus and Russia and of China, except to mention that Marco Polo commented on the frequency of cervical tumours among the inhabitants of the high Pamirs and the Yarkand during his famous journey from Venice to the court of the Grand Kahn in China about the year 1275. He also ascribed these tumours of the throat to the quality of the water drunk by the inhabitants.

Coming to Japan the picture is entirely different. The Japanese not only consume large quantities of fish but they also eat sea-weed. As a result, simple goitre is practically non-existent in Japan. McClendon (1939), for example, could find only four cases of goitre among 20,000 inhabitants examined. It is noteworthy that 10 grammes of dried seaweed, an amount often taken at a single meal, contain about five milligrammes of iodine, or enough to supply normal requirements for nearly two months.

Now, reverting to iodine prophylaxis, it is clear that the purpose of thyreoid hyperplasia is to increase the gland's ability to extract iodide from the plasma. If the plasma iodide level is high such adaptive hyperplasia is unnecessary.

It may be stated categorically that there is no endocrine disease which can be so easily and so surely prevented as simple goitre. All we have to do is to ensure an adequate supply of iodine in the daily dietary, and that such prophylaxis works in practice has been shown conclusively wherever it has been tried. Figure III summarizes data on the efficacy of iodized salt, showing the goitre incidence in school children and recruits in the years before and after the introduction of iodized salt. Iodization of salt is now almost universally recognized as the most convenient and effective method of goitre prophylaxis, since it requires no special effort on our part, salt being an invariable constituent of the diet.

What are the sources of iodine, and how much of it should be added to the salt? In only one place in the world is iodine found in quantity and that is in a grim and desolate plateau in northern Chile. There, in the lifeless Nitrate Desert, 3000 feet above sea-level, is produced over 80% of the world's iodine supply. In this region there are inexhaustible deposits of nitrate of soda rock, containing about 0·1% of iodine, which is recoverable as a by-product during extraction of the nitrates. It is interesting to

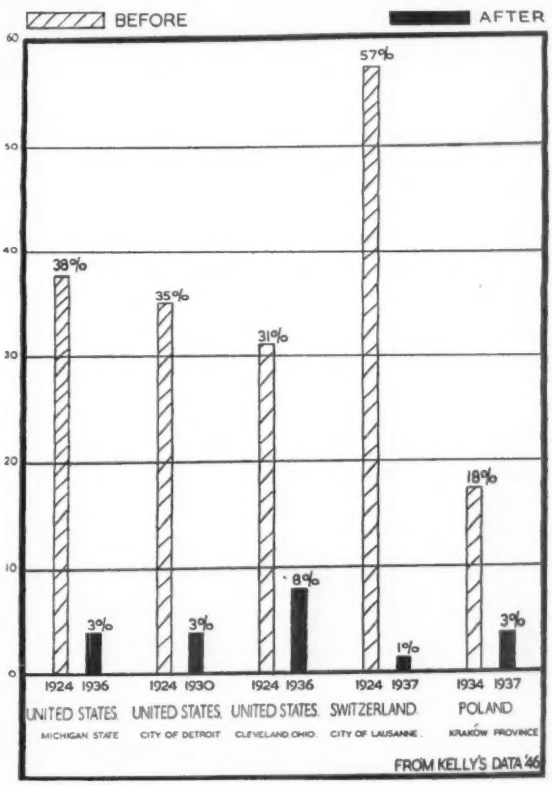

Figure III.

Goitre incidence before and after the introduction of iodized salt.

speculate how these vast deposits of nitrate of soda came to be laid down in Chile. It is thought that long ago an inland sea containing great masses of seaweed was thrown up by volcanic action. Subsequently its waters evaporated and vast beds of decaying organic matter were converted into nitrate by the action of nitrifying bacteria.

The proportions of iodide officially recommended in various countries are shown in Table II. It will be seen that they roughly fall into two groups: those of the United States, Canada and New Zealand, and those of the European countries, which are about ten times lower. Physiologists estimate that the daily iodine requirement is only 100 to 200 microgrammes, or about one milligramme a week, so an intake of 50 milligrammes annually would theoretically be sufficient. From estimates of the average amount of salt eaten daily in the United States, it is calculated that one in 10,000 parts of potassium iodide will give an annual intake of 200 milligrammes, or four times the minimum theoretical requirement. The quantity of iodine given is still quite small and no harm comes from this excess.

Are there any dangers in iodine prophylaxis? There have always been some medical critics of iodine prophylaxis, especially in Europe. These doctors have stated that the iodization of salt favours over-production of thyreoid hormone in a person whose gland is already hyperplastic. So-called iod-Basedow or iodine thyreotoxicosis is thus produced.

Fortunately practical experience has shown that these fears are groundless. In fact, there is no clear proof that iodine-induced thyreotoxicosis exists as a clinical entity. Indeed, there is evidence (Wolff and Chaikoff, 1948) that the blood iodide level acts as a homœostatic regulator of thyreoid function. If this level is abnormally high —namely, above 20 microgrammes *per centum*—hormone synthesis and therefore secretion are blocked. Incidentally, this may explain the therapeutic effect of Lugol's iodine in thyreotoxicosis.

Residual Goitre.

Even with adequate iodine prophylaxis there is always a residual incidence of simple goitre in endemic areas (Figure III). The importance of sex in the ætiology of simple goitre has already been mentioned, and unknown individual and familial factors probably play a role. Nevertheless, some doubt has been cast on the influence of heredity in simple goitre by the work of Martin and Fisher (1945), it being suggested that the frequent occurrence of simple goitre in the same family may depend on their all being exposed to the same exogenous cause—for example, iodine deficiency.

Iodine-deficiency goitre depends, of course, on compensatory thyreoid hyperplasia. In a different category are the goitres depending on frustration hyperplasia, resulting from the ingestion of agents which block hormone synthesis. Anti-thyreoid compounds which cause goitre ("frustration hyperplasia") in man by blocking hormone synthesis may be set out as follows: (i) those containing a thiocarbonamide group, which include the thiouracils and thiooxazolidone; they are potent in man, rabbits, rats *et cetera*; (ii) derivatives of aniline including sulphanilamide and sulphaguanidine—potent in rabbits and rats but not in man; (iii) potassium thiocyanate, which is goitrogenic in man; it paralyses iodide uptake; its action is counteracted by excess of iodine. Though the precise explanation of residual and sporadic goitre remains obscure, Astwood and his group in Boston have recently produced suggestive evidence of a possible dietary factor in explaining some at least of these goitres. They have found that yellow turnips and other vegetables contain quite a powerful anti-thyreoid agent, and this, by blocking hormone synthesis at the same stage as thiouracil, may lead to "frustration hyperplasia" and goitre. Cooking the turnips destroys their anti-thyreoid effect. The agent responsible is thiooxazolidone. It has now been isolated and synthesized. It contains the same thiocarbonamide group as thiouracil. It has slightly more anti-thyreoid potency than propyl thiouracil. Thiooxazolidone has been identified in turnips, cabbage, kale, Brussels sprouts, broccoli and kohlrabi.

Greer, Ettlinger and Astwood (1949) conclude that it is unlikely that the quantities of these foods eaten normally will produce goitre, but if, as sometimes happens, the diet is limited almost entirely to turnips and other vegetables, thyreoid enlargement may be produced.

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Reports of Cases.

ABDOMINAL MIGRAINE: REPORT OF A CASE.

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MIGRAINE, in its protean forms, is a symptom-complex usually dominated by headache. Among the array of migrainous variants abdominal migraine is one of the rarest. Slight and Morisson, in an investigation of 169 cases, found variants in 30, and among these two patients showed abdominal crises replacing migraine. The case reported below began as one of so-called cyclical vomiting in childhood, and the symptoms, persisting into adult life, displayed the characteristic syndrome of abdominal migraine.

Clinical Record.

N.H., aged sixteen years, had experienced attacks of vomiting since the age of three years. The attacks of vomiting that she remembers last about one week and then clear up for one or two weeks. This cycle is repeated for two to six months and then she does not vomit again for about two years. During the attacks she loses her appetite and becomes constipated and thirsty. Several attacks have required admission to hospital. The day before the attack she becomes fatigued and listless, and the next morning she wakes up vomiting. She has never experienced headaches, visual disturbances, paræsthesiæ *et cetera*, and the vomiting has never been associated with abdominal pain. Her family history reveals that her two brothers and father experience migraine, and there is no history of epilepsy or of allergic disorders.

Physical examination of the patient revealed no abnormal signs. A barium sulphate meal examination made before her admission to hospital during an attack revealed gastric dilatation and delayed emptying. Also before her admission to hospital the therapeutic effect of "Gynergen" was tried, and on three occasions it stopped the attacks in a few hours, whereas usually they lasted for one week. While in hospital she was symptom-free, and a barium meal examination showed the stomach to be of normal size and to empty normally. A normal curve was obtained from a fractional test meal examination. The electroencephalogram showed minor abnormalities of a generalized nature.

Comment.

Buchanan in 1921 reported the first cases of abdominal migraine, and Brams in 1922 and Brams and Blitzsten in 1926 reported other cases, the last-named authors dividing cases of abdominal migraine into three groups. First, there were cases of paroxysmal abdominal pain with or without cephalalgia. Secondly, there were those in which typical migraine was followed by abdominal symptoms. In the third or larval type abdominal pain was mild or absent and nausea and vomiting predominated. It is in this larval type that diagnostic difficulties arise. Hunt, discussing bilious attacks, describes the features of abdominal migraine as follows. Attacks occur at intervals, sometimes quite irregularly and with no apparent cause, often following emotion or mental excitement. They begin commonly in early adult life and are frequently preceded by a day or two of preliminary depression or lethargy, which is followed by abdominal discomfort or actual pain and succeeded by vomiting. Giddiness is frequently present, but no pyrexia, and the state of misery and depression is very different from the frightened, shocked attitude of patients with an acute abdominal catastrophe. The migrainous nature of the attacks may also be suggested by a family history of migraine, by the absence of signs of organic nervous disease, by the presence of hemicrania, by the relief produced by vasoconstrictor drugs, by an abnormal electroencephalographic tracing and by the non-progressive history.

Dow and Whitby, in a study of 51 cases of migraine, found a persistently abnormal electroencephalogram in 30. Of these, in 14 a generalized non-specific dysrhythmia was present, and in 12 a localized unilateral abnormality. Strauss and Selinsky found an abnormal electroencephalogram in 9 of 20 cases during the headache, but in only four was the tracing abnormal between attacks, and two of these subjects were also epileptic.

Grieg postulated that migraine was due to recurrent attacks of dilatation of the stomach; but Hurst stated that he had found nothing to support this. It is interesing that the present patient showed gastric dilatation during the attack.

Cyclical vomiting in childhood is often followed by migraine in later life (Brain, 1947; Holt and Howland, 1916), and epilepsy is more common in patients with migraine than in the general population (Critchley and Ferguson, 1933). The association of cyclical vomiting with migraine is further suggested by the fact that nausea and vomiting in young adults may occur prior to the development of migraine (Critchley and Ferguson, 1933), and a family history of migraine is common in children with cyclical vomiting (Dods, 1935). Also in young children the headache of migraine may be a minor feature, but nausea and vomiting may be pronounced symptoms (Mitchell and Nelson). There appears to be no clear dividing line where cyclical vomiting of childhood ends and the abdominal variant of migraine begins.

The functional pathology of abdominal migraine is obscure. Moore, in a critical analysis of abdominal migraine and abdominal epilepsy, states that the abdominal symptoms are due to discharges arising in cortical areas 6, 5 and 3 of Brodmann, or in the diencephalon, or in both, which produce abnormal motility of the intestinal tract with resultant pain. He stresses the importance of this syndrome as a clinical entity and urges that it be called abdominal epilepsy and not abdominal migraine.

Summary.

1. A case of abdominal migraine is reported. It appears to demonstrate the similarity between cyclical vomiting of childhood and the abdominal variant of migraine.

2. The diagnosis and functional pathology are discusesd.

Acknowledgements.

I wish to express my thanks to Dr. A. W. Morrow, honorary assistant physician, Royal Prince Alfred Hospital, for permission to report this case, and to Professor C. G. Lambie and Professor Lorimer Dods for their helpful suggestions in the preparation of this article.

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A CASE OF HEMIPARESIS FOLLOWING CUT THROAT.

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The Accident.

ON Friday, July 13, 1951, a patient, tiring of life's fitful passage, attempted to "end it all" by stabbing himself in the neck with a table-knife. He was found lying "in a pool of blood" with the knife protruding from his neck. He was bleeding profusely from the wound. The bleeding was venous. An effort had been made to stem the flow by digital pressure. It was difficult to assess the amount of blood lost. The patient was unconscious; the unconscious state of the patient could not be explained by the loss of blood, and the only suggestion that can be applied is that the over-energetic digital hæmostasis had caused partial strangulation or interruption of the cerebral blood supply, but his pulse was full and steady to the palpating finger. His colour was good. Slow, lateral oscillations of the eyeballs were noted. The pupillary reactions were normal. The retinal vessels were observed to be normal.

The Wound.

The wound was about one and a half inches in length, and situated about four inches from the sterno-clavicular origin of the sterno-mastoid muscle, and on the outer border of the latter. Alongside the main cut, and at its lower end, one could see a tiny tentative cut. First-aid hæmostasis had been accomplished by thrusting an artery forceps into the wound and clamping a large bite of tissue. The small size of the wound rendered accurate identification of bleeding points difficult. Later it was evident that, to a large extent, the clotting mechanism had played a major part in the hæmostasis; a most profuse hæmorrhage followed an attack of coughing which dislodged the clot.

The knife had passed into the neck to a depth of some four and a half inches. On palpation of the larynx, crepitation could be felt, indicating damage to that structure.

The Treatment.

After the second profuse hæmorrhage steps were taken to enlarge the wound in the line of the vessels. This was done to the extent of four inches. The underlying tissues were grasped with a number of forceps. No attempt at dissection was made because of the hæmorrhage and because of a sudden change in the patient's condition which now became apparent. The pulse had become rapid and of poor volume. One millilitre of "Coramine" was administered intramuscularly. It was decided that the best course of action was to insert some deep sutures of catgut on a large curved needle (an earlier attempt had been frustrated by a small needle breaking off deep in the tissues), in the hope that the severed vessels would be included in the ligature. This was done. The hæmorrhage ceased. To add to the joy of accomplishment, the fragment of broken needle turned up just as the skin sutures were being inserted.

But now the patient developed Cheyne-Stokes respiration. Hurriedly one millilitre of "Coramine" was administered intravenously, followed by one millilitre of adrenaline at a more leisurely pace. A few minutes elapsed and nothing seemed to happen. Then the patient had what appeared to be an attack of bronchial spasm, lasting for a few seconds and followed by an attempt to vomit. Again he was peaceful. Then he had another spasm, after which his respirations and pulse improved. His blood pressure, which could not be recorded a few minutes earlier, began to rise and soon nearly approached normal. Oxygen was now given. The patient was returned to the ward. One pint of serum was administered. Penicillin was given, 50,000 units every four hours, as a prophylactic measure. He was still unconscious and had been for some three and a half hours.

The Patient.

The patient, aged thirty years, had been prior to this attempt on his own life a strong, well-built, athletic man. He was admitted to hospital as a schizophrenic. He had made two previous attempts on his life, once with strychnine and once by cutting the vessels of his arm.

The Result.

Four days after this attempt (July 17) his temperature rose to 104° F. The patient was flushed and restless. His pulse was rapid and full. The decubitus was that of cerebral irritation. The lungs were clear. Slight neck rigidity was demonstrated, the wound of the neck being kept in mind. Kernig's sign was elicited on both sides. Contralateral flexion of the legs was elicited. The plantar response was extensor in type (Babinski) on the left. The knee jerks were increased. It was decided to perform a lumbar puncture. This revealed increased pressure. (A manometer was not used; the pressure was judged by timing of the rate of drop.) Macroscopic examination of the cerebro-spinal fluid showed it to be clear; the globulin content was not increased. The protein content was 25 milligrammes per 100 millilitres and the chloride content was 708 milligrammes per 100 millilitres. No cells were found. On microscopic examination of the fluid no organisms were seen, and on culture no growth was obtained.

The patient's temperature dropped and his condition improved a few hours after the puncture. The penicillin therapy, which he was still having, was reinforced by the addition of sulphathiazole.

A few days later it became apparent that the patient was suffering from dysarthria. At the time the damage to his larynx was blamed. Then it became clear that he had developed left-sided facial paralysis. Careful examination revealed that it was part of a left-sided hemiparesis. There was little or no power in the left leg; the knee jerks were fairly brisk. The calf and thigh muscles were soft and flabby to the touch. The left arm was completely powerless; the biceps and triceps jerks were of moderate quality. These muscles, like those of the leg, were flabby to the palpating fingers. The hand was beginning to present a wasted appearance. Babinski's sign was still very pronounced on the left side. Difficulty was experienced in eliciting Kernig's sign, which rendered the result uncertain, although there was a suggestion of muscle spasm. Lack of cooperation from the patient made the testing of sensation impossible. At the same time incontinence of urine made its entrance on the stage. Now, three weeks after the accident, there are few signs to suggest the possibility of a complete recovery.

The object of this case report is to ask how this hemiparesis was produced.

The Enigma.

1. Did we ligate the internal carotid in our effort to arrest the hæmorrhage and, if so, would this cause the hemiparesis?

2. Could the condition have been caused by a retrograde thrombosis?

3. Would the complete destruction of the venous drainage of the right-hand side cause slowing of the cerebral circulation to a degree sufficient to cause œdema, and would this œdema, if confined to the right side, cause left-sided hemiparesis?

4. Could we have damaged the vagus nerve with our instrumentation, and could this damage give rise to ascending myelitis with resulting hemiparesis?

The Conclusion.

It is hoped that the facts are sufficiently clearly set out to allow for the comment which is looked for.

Reviews.

A TEXT-BOOK OF MEDICINE.

CECIL'S "Textbook of Medicine" was first published in 1927. It is now appearing in its eighth edition, for the first time bearing the name of Loeb along with Cecil.[1] Many new subjects have been added to this edition, though it is 136 pages shorter than the previous one. The two editors have been assisted in this large work by three associate editors. Treatises have been written by 168 authors, several of whom are well-known American physicians. The first section of the book deals mainly with diseases from the ætiological standpoint. Following this the chapters are concerned with the diseases occurring under different systems.

The scope of the book is most exhaustive, and there can be no subject or disease which is not described somewhere in the book. Each disease is well set out, the account starting with a definition, going on to ætiology, pathology *et cetera* and working through to treatment. Sections on most diseases are also followed by a list of references. It is thus extremely easy to use this book for reference even if one wishes to study one portion of a given disease only. Although the title of each reference is given, it is a pity that note is not made to these in the text.

The illustrations and tables assist much in the understanding of the text, though these days with the emphasis on visual education, one feels that the further use of illustrations and diagrams would be helpful.

The type used in this edition is clearer than that used in the seventh edition. The current American system of two columns to each page is used. The index is particularly good, and well set out, with the main pages dealing with a particular subject in heavy type.

A few criticisms may be made. When text-books of medicine were first published they were written by one author only. As the subject has now become so immense it is impossible for the average author to cope alone with

[1] "A Textbook of Medicine", edited by Russell L. Cecil, M.D., Sc.D., Robert F. Loeb, M.D., and associate editors Alexander B. Gutman, M.D., Walsh McDermott, M.D., and Harold G. Wolff, M.D.; Eighth Edition; 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" × 7½", pp. 1658, with 204 illustrations, a few in colour. Price: £5 14s.

a whole text-book of medicine When many authors contribute to a book an essential unity tends to be lost and one feels therefore that the smaller the number of contributors the better. With this book, although many of the contributors are world famous, it is not reasonable to suppose that the whole one hundred and sixty-eight are equally capable. When one reads the book one tends to find some inconsistencies when overlapping diseases are described by different people. We wonder whether some authors have been asked to give small contributions so that their names, world famous, could appear on the list of authors.

As in many text-books of medicine there is a tendency in diagnosis to place laboratory aids before clinical features. Admittedly in many diseases one requires bacteriological examination to establish or confirm a clinical diagnosis. However, in practice it is the history and physical examination which lead one in the first instance to the diagnosis. Because of the tendency of modern medical students and practitioners to rely on ancillary aids, text-books of medicine should discourage this attitude and stress basically the clinical features of disease in diagnosis.

Again, in treatment the general treatment is often poorly done, whereas complicated treatment applicable to a few cases is done in greater detail. For instance, in asthma the treatment starts with the treatment of the attack and severe intractable asthma and later comes on to basic treatment, but at no stage deals with the psychological aspects of this disease. It is common experience that for every attack a practitioner has to treat he is confronted with five to ten patients seeking treatment between attacks, and in these cases a study of the psychological basis is most profitable. In bronchiectasis we are told that the treatment of choice is lobectomy, and only after a discussion on the surgery of bronchiectasis are we told about the much more generally useful regime of postural drainage.

The subject of nephritis is dealt with by Professor Loeb himself, but it is strange that no mention whatever is made of the clinical classification of Ellis, which in British countries is now taken as the standard working basis for a study of the natural history of nephritis.

In spite of these criticisms we think that this text-book of medicine will remain one of the standard works with medical students and practitioners, mainly for reference purposes. The editors and publishers are to be congratulated on producing a new edition with so much new material, which is remarkably up to date.

AN ATLAS OF SURGICAL PATHOLOGY.

Dr. Karl T. Neuberger, Professor of Pathology at the University of Colorado School of Medicine, Denver, Colorado, has compiled an "Atlas of Histologic Diagnosis in Surgical Pathology".[1] It is a large well-printed volume containing 880 photomicrographs in black and white, each of which is accompanied by a concise and accurate description. The photomicrographs were made from routine biopsies of tissue removed at operation; necropsy material was used only occasionally. Some are very good, but on the whole they are of only fair average quality; many are too dark and the contrast is often poor. It is surprising that colour photography, so widely used nowadays, finds no place in this atlas. Most of the material was derived from the surgical accessions of the Colorado General Hospital and from the author's own slide file. The collection is a very good one and it is clear that the author is a most capable and experienced histopathologist. But it is equally clear that such knowledge and experience as his cannot be passed on by an atlas of photomicrographs. There are many branches of medicine that cannot be learnt from printed books, and histopathology is one of them. It is a well-recognized fact that the tiro must learn this art from a master of it, slide by slide, tissue by tissue, one might almost say cell by cell, and an atlas of one's own in the form of a collection of tissue slides must be compiled. The appearances seen under the microscope are not easily or exactly captured in a black and white, or even in a coloured, photograph. Doubtless the author presupposes some knowledge of pathology in those who will use the book, and his collection will be of interest to other experienced pathologists. In his preface the author advises that the atlas should be consulted when a diagnosis is in doubt. This is dangerous advice; and the advertisement "blurb" on the inside of the paper cover-jacket is really reprehensible. Part of it reads: "When you must make a histopathological diagnosis, of whatever part of the body, you are sure to find it amply covered in this atlas. Study the large clear photomicrographs, grasp the essential facts from the text beside them and proceed with confidence to successful differential diagnosis." That is not the way to do histopathology. This atlas is a project that has been carried out well and painstakingly; but the idea underlying it is open to serious criticism.

[1] "Atlas of Histologic Diagnosis in Surgical Pathology", by Karl T. Neuberger, M.D., with a section on Exfoliative Cytology by Walter T. Wikle, B.S., M.S., M.D.; 1951. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10" × 7", pp. 470, with 880 photographs. Price: £5 18s. 3d.

PITUITARY HORMONES.

We are accustomed to regard the hypophysis as the supreme executive in the endocrine hierarchy, and yet our knowledge of the trophic hormones by which it directs the activities of subordinate glands is all too meagre. In *"Les stimulines hypophysaires"*, by three French authors, an admirable account has been written of what little has been discovered in this really vast field.[1] If the reader expects undue emphasis to be placed on French researches he will be agreeably disappointed, for if there is discrimination at all it is in favour of American work. The subject is a difficult one because the hormones released by the pituitary gland are of protein character and, in consequence, their purification is difficult, their storage beset with pitfalls and their synthesis at present impossible. Perhaps the one protein product studied in detail is the growth hormone which has been broken down into its constituent amino acids and has had its molecular weight (about 47,000) calculated and estimated. The authors point out that extensive use is being made of the hormones liberated by the adrenal gland and by various reproductive organs, but that little attention has been directed towards the therapeutic use of the activators emanating from the pituitary gland. This is a perfectly fair critical comment and one must really blame the imperfect state of our knowledge of pituitary hormones for this neglect. Logically one should use hormone therapy operating through the pituitary; also there is always the possibility of "back lash" on the head organ when the hormones lower in physiological status are injected. Every regulatory action of the hypophysis is brought under review with that pellucid clarity of exposition we expect from French authors. The problem of antihormones is well discussed and also the neural mechanisms of the pituitary being set in action by sensory impulses—that dealing with visual stimuli is particularly good. The authors are cautious about the formation of the neoplasms, but are inclined to think that the pituitary acts as an intermediary. Extirpation of the hypophysis slows the development of certain tumours or actually prevents their occurrence. Conversely injection of pituitary extracts facilitates the formation of certain tumours. Authors and publisher are to be congratulated on a very fine book which is both stimulating and helpful.

[1] *"Les stimulines hypophysaires"*, by André Lemaire, Florian Delbarre and J. P. Michard; 1951. Paris: Masson and Cie. 10" × 6½", pp. 172. Price: 750 fr.

ENZYMES AND ENZYME SYSTEMS.

"Enzymes and Enzyme Systems" is made up of six contributions by active workers in the field of enzymology originally prepared for seminars at the University Laboratory of Physical Chemistry Related to Medicine and Public Health of Harvard University.[2] They all have to do with the association of enzyme systems with proteins. This is a book for the specialist in enzymology as will be seen by the nature of the subjects discussed. The contributions will be considered in order.

"The Organized Respiratory Activity of Isolated Rat-Liver Mitochondria" by A. L. Lehninger deals with oxidation of fatty acids by isolated mitochondria, the relation of this to the Krebs cycle and the presence within the mitochondria of all the enzymes associated with the citric acid cycle.

"The Cyclophorase System" by David E. Green treats of the enzyme systems associated with the citric acid cycle, fatty acid oxidation and oxidative phosphorylation in particulate material isolated from cells, probably mitochondria. The important concept developed is that the unit of the system of enzymes studied is no longer the individual

[2] "Enzymes and Enzyme Systems: Their State in Nature", edited by John T. Edsall; 1951. Cambridge, Massachusetts: Harvard University Press. 8½" × 5½", pp. 160, with 29 figures. Price: 31s. 6d.

enzyme, but a hierarchy of enzymes, and that the individual enzymes in such a system have properties not demonstrated by the individual enzymes.

"Aspects of Specificity and Mode of Action of Some Peptidases" by Emil L. Smith considers the relation of certain peptidases to metallic ions, manganese, cobalt and magnesium.

"The Reactions of Horseradish Peroxidase with Various Hemins" by Andreas C. Maehly deals with the replacement of the normal hæmin in peroxidase by other hæmin or hæmin-like substances.

"The Reaction of Ferrocytochrome-C with Peroxidases and Peroxides" by Britton Chance is a highly technical discussion on the subject of the title.

"The State in Nature of Proteins and Protein Enzymes of Blood and Liver" by Edwin J. Cohn, Douglas M. Surgenor and Margaret J. Hunter is an extensive account of the separation of protein fractions from blood and liver by very mild chemical procedures and the distribution of enzymes in the various fractions.

EYE MANIFESTATIONS OF INTERNAL DISEASES.

THE third edition of "The Eye Manifestations of Internal Diseases" by I. S. Tassman has been enlarged to include much new material.[1] The section on glaucoma has been rewritten "in order to conform to the present-day understanding of this condition". After this introduction, it is surprising to read that: "The immediate local cause of glaucoma is an obstruction of the angle of the anterior chamber." This is an over-simplification of a problem which is the bane of all ophthalmologists, and is a poor introduction to a general discussion on the disease. The author is more at home with his survey of current opinion, and retrolental fibroplasia. This book will be appreciated by the reader accustomed to gleaning his information from the digest magazines.

AN OUTLINE OF FRACTURES.

THE third edition within ten years of "A Complete Outline of Fractures, Including Fractures of the Skull", by J. Grant Bonnin, is modestly described as limited to the use of the undergraduate and post-graduate student.[2] In the true sense, we remain post-graduate students to the end of our days. This edition is an indication of the book's fulfilment, and of its retention of an assured place in its nominated field; the connoisseur will find much of interest, particularly in the wider exposition on injuries to the ankle, which the author has made his particular work. Increase in size results from this and from the inclusion of recent further fracture work such as use of the Küntscher nail, and the operative treatment of hand and finger injuries and the use of antibiotics.

An intelligent approach is facilitated by the inclusion of surgical anatomy and development at the beginning of each chapter.

With the addition of appendices on the organization of a fracture clinic and the surgical exposure of the long bones, encouragement is given to the goal of general attainment of unity of control in fracture work. The manner of writing is lucid and the book is a fund of valuable clinical observation and practical advice, and it bears a desirable imprint of the author without detraction from accepted methods.

The illustrations and diagrams are in general well done (Figure 490 would probably not be accorded general acceptance). The persistence, however, of what was a minor blemish in early editions into the third edition may result from publication difficulties. But the proof-reader might see that the well-known condition of "osteochondritis dissecans" is not miswritten four times as "osteochondritis dessicans", in view of the etymological significance.

In its efficient organization, methodical and accurate approach, clarity of expression and general excellence, the book has now reached a stage at which the author might consider whether this complete outline should not at some future date merge into a complete work on fractures.

[1] "The Eye Manifestations of Internal Diseases (Medical Ophthalmology)", by I. S. Tassman, M.D.; 1951. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9½" × 6½", pp. 672, with 279 illustrations, including 25 in colour. Price: £6 6s.

[2] "A Complete Outline of Fractures Including Fractures of the Skull for Students and Practitioners", by J. Grant Bonnin, M.B., B.S. (Melbourne), F.R.C.S. (England); Third Edition; 1951. London: William Heinemann (Medical Books), Limited. 8¾" × 6", pp. 686, with 710 illustrations. Price: 42s.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Anesthesia in General Practice", by Stuart C. Cullen, M.D.; Third Edition; 1951. Chicago: The Year Book Publishers, Incorporated. 8" × 5½", pp. 292, with 36 illustrations. Price: $4.50.

The second edition was published in 1948.

"Handbook of Diseases of the Blood", by A. Piney, M.D., M.R.C.P.; 1951. London: Harvey and Blythe, Limited. 9" × 6", pp. 224, with 11 illustrations. Price: 21s.

An attempt to depict hæmatology as a primarily "bedside" subject.

"The Unconscious Significance of Hair", by Charles Berg, M.D. (London), D.P.M.; 1951. London: George Allen and Unwin, Limited. 9" × 6", pp. 112. Price: 15s.

The book is "a psychiatric criticism of normality based upon a chosen item of typically normal behaviour".

"Modern Trends in Pædiatrics", edited by Sir Leonard Parsons, M.D., F.R.S., F.R.C.P.; 1951. London: Butterworth and Company (Publishers), Limited. 10" × 7", pp. 612, with 113 illustrations. Price: 80s.

A member of the "Modern Trend Series", comprising 21 articles by different authors.

"Review of Physiological Chemistry", by Harold A. Harper, Ph.D.; Third Edition; 1951. Palo Alto, California: University Medical Publishers. 10½" × 7", pp. 268, with 13 figures. Price: $3.50.

The book is "intended as a supplement to the standard texts in biochemistry and as a companion volume for the student in such courses".

"Diseases of Infancy and Childhood", by Wilfrid Sheldon, M.D. (London), F.R.C.P. (London); Sixth Edition; 1951. London: J. and A. Churchill, Limited. 9" × 6", pp. 824, with 23 plates (four in colour) and 182 test figures. Price: 40s.

Intended to be "something more than a mere handbook, and yet in no sense competitive with the larger works of reference".

"The Story of St. Luke's Hospital", by Brigadier C. N. French, C.M.G., C.B.E., with a foreword by Sir George Cockerill, C.B.; 1951. London: William Heinemann (Medical Books), Limited. 9" × 5¾", pp. 220, with eight illustrations. Price: 8s. 6d.

The author was for a time secretary of the hospital and carried out research in the records of the institution.

"Notes for Introductory Courses in Genetics", by Charlotte Auerbach, Ph.D., D.Sc.; Third Edition; 1951. Edinburgh: Oliver and Boyd. 7½" × 5", pp. 42. Price: 2s.

The object of the book is to help students who attend courses in elementary genetics.

"The Amino Acid Composition of Proteins and Foods: Analytical Methods and Results", by Richard J. Block, Ph.D., and Diana Bolling, B.S.; Second Edition; 1951. Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 10" × 6½", pp. 614, with eight illustrations, 31 charts and six diagrams. Price: 75s. 6d.

The object of the authors is to present to the average reader the widely scattered literature on the methods and results of protein analysis in the most easily usable form.

"Newer Concepts of Inflammation", by Valy Menkin, M.A., M.D.; 1951. Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 9" × 6", pp. 154, with 67 illustrations. Price: 25s. 6d.

Intended to focus attention on the biochemistry of the injured cell.

The Medical Journal of Australia

SATURDAY, OCTOBER 6, 1951.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

VIOLENT AND UNEXPLAINED DEATHS: THEIR INCIDENCE AND INVESTIGATION.

WHETHER the members of the medical profession realize it or not, they are in no small degree the guardians of the public in the matter of death. If a practitioner has been in attendance on a patient shortly before death and if he can certify that death is due to a recognized disease process, he is entitled to give a certificate on a form provided for the purpose. If death has been due to violence or if the cause is obscure, a report must be made to the coroner, who may either give an order for burial or have some special inquiry made. The practitioner's responsibility is considerable and any failure on his part may cause inconvenience to the public and, conceivably also, a miscarriage of justice. This, the responsibility of the practitioner, is one side of the picture; on the other side is the responsibility of the State to discover the cause of death and take appropriate action. According to the "Official Year Book of the Commonwealth of Australia" for 1946-1947, the total number of deaths in Australia during 1946 was 74,661; the number of violent and unexplained deaths was 6692. These are grouped under the following headings: suicide, 2558; homicide, 90; automobile accidents, 1206; other violent or accidental deaths, 2606; legal executions, 2; ill-defined and unspecified deaths, 228. The 6692 deaths represent nearly 9% of the total number. We do not propose to discuss these groups individually, interesting though such a discussion would doubtless be. Rather would we consider the Australian position in the light of an article on the medico-legal investigation of violent and unexplained deaths presented by Richard Ford to the Section on Pathology and Physiology at the annual meeting of the American Medical Association at San Francisco in June, 1950.[1] In the discussion on Ford's paper L. J. Regan said that 20% of all deaths in the United States resulted from violence or occurred unexpectedly from obscure causes. The number each year was about 300,000. He went on to say that each year from 13,000 to 14,000 murders were officially recognized, or one murder each year for every 10,000 living persons. (The corresponding Australian figure for 1946 would be one murder for approximately every 83,000 persons living.) Ford states in his opening sentence that the competent supervision in the public interest of violent and unexplained deaths requires above all the guidance of medical investigators, familiar with the community and trained to appreciate and preserve collateral evidence at the scene of a crime. His arguments and the illustrative cases which he describes in some detail give good support to his contention. His opinions are supported by the surprising statement made by L. J. Regan that medical science participates less effectively in the administration of justice in the United States than it does in any comparable civilized country in the world. Ford holds that the medical investigator envisaged by him should be concerned with the acquisition of medical evidence coordinated with other physical evidence, with the aim of establishing the true cause and manner of death. Another requirement in his opinion is the establishment of one or more central laboratories capable of providing the medical investigators with consultants and technical experts. On reading this, those who are familiar with the crime novels of the late R. Austin Freeman (a medical practitioner) will think at once of his life-like and entirely creditable creation John Thorndyke with his crinkly-faced technician Polton. Though Thorndyke's pathology belongs to that of a decade or two ago, it is sound, and may well be mentioned in such a serious discussion as that of Ford and others at the American meeting. Ford mentions automobile accidents; 32,000 were recorded in the United States in 1948. He explains that in most parts of the country the body of the victim is rarely examined to determine whether responsibility should be shared by or placed on the victim because of his drunkenness, disease or medication. A boy, aged nine years, was run over and killed by a trackless trolly. Inquiry revealed that the boy had been "cured" of tuberculous meningitis by streptomycin and at autopsy atrophy of the entire right occipital lobe of the brain was found. This would produce left homonymous hemianopsia and actually the boy had been unable to see the vehicle as it was coming towards him—the blame for the accident did not rest entirely on the driver. Under the heading of homicide Ford describes three cases in which careful medical evidence established the guilt of a suspect. He also gives details of three cases in which innocent persons were exonerated—in his opinion the most important function of medico-legal investigation. In regard to "public health and safety" the medico-legal investigator can be a protector when sudden death is found to be due to diphtheria or pulmonary tuberculosis; Ford emphasizes this fact and also refers to deaths from carbon monoxide poisoning revealed by post-mortem examination. The work of K. M. Bowden, of Melbourne, on supposed suffocation of infants, published in this journal, shows how valuable from the public point of view a trained investigator can be.

This whole subject is clearly of great importance. Whether medical investigators are used to the best advantage in the United States is a matter for the individual State authorities in that country. For Australia we may say—and it will be true for all countries—that the oftener complete and careful post-mortem examinations are carried out when the cause of death is not certain or when the responsibility or blameworthiness of any person or group of persons is in question, the less likely is error to occur. Only when medico-legal considerations arise in relation to

[1] *The Journal of the American Medical Association*, April 7, 1951.

a death is the life or liberty of an individual in jeopardy because of State action. As a rule the legal aspect of a case or the possible existence of such an aspect will be obvious; but ordinary disease may cloak a murder and what appears to be homicide may be a death due to disease. It is as a rule on the coroner that the burden of ordering post-mortem examinations must rest. Were coroners all trained in medicine as well as in law, conditions would be more satisfactory than they are. No doubt coroners obtain expert medical advice when they think they need it, and if they have not developed a self-satisfied routine this may be sufficient. Ideally some of the decisions made by a coroner should be made by a highly trained pathologist who has legal insight. We do not necessarily require the regional appointment of a Public John Thorndyke, but we can agree with Richard Ford when he states on the one hand that a good pathologist would make a good medical examiner, if he was conscious of the special problems of the field of legal medicine, and on the other that there is no such thing as a complete medical examiner who is not a good pathologist.

Current Comment.

THE ACTION OF MORPHINE ON THE INTESTINE.

Interest in the mode of action of morphine in producing its side effects has been sharpened since the introduction to clinical usage of some of its now well-known substitutes. This in turn has turned attention to the pharmacological problems involved, some of which have never been clearly settled. The most important side effect is that upon the intestinal muscular function. This was the subject of work some time ago by E. M. Vaughan Williams and D. H. P. Streeten, and these investigators have now amplified their experimental work and produced supporting evidence for the hypotheses advanced.[1] Numerous studies by others have shown that morphine causes an increase of "tone" in the intestine, though this term perhaps begs the question somewhat, for it is rather that the drug causes a contraction of an intestinal segment sufficiently sustained to bring about movement of a balloon or its contents or to accelerate the passage of an artificial bolus within the lumen of the bowel. In spite of this early effect the main action of the drug on the intestine is in the end a prolonged slowing of the rate of propulsion of these imitations of the usual contents of the bowel, as has been clearly shown by radiological observations in human and other animal subjects.

Vaughan Williams and Streeten point out that actual surgical observations have also shown that active contractions of the intestine have been seen following the administration of morphine. Their own previous work demonstrated that the degree of change in propulsion or transport of fluid in cannulated loops of intestine could be measured under experimental conditions, and that the results suggested failure of propulsion due not to paresis of the intestinal muscle, but to a sustained contraction which closed the lumen and thus prevented coordinated muscular movements. The experimental technique was relatively simple. A short loop of intestine was isolated from the alimentary tract of a dog and the blood supply and nervous connexions were left intact; "Perspex" cannulæ were introduced at each end of the loop, which remained within the abdominal cavity. Tyrode solution was allowed to pass through the loop with the animal conscious, and the animal had no discomfort after recovery from the procedure; pressure and height of this fluid above the reservoir allowed the rate of transport to be measured. The side effects of morphine could thus be estimated and compared with those of substitute drugs, in particular pethidine and amidone, and the action of antagonists such as atropine was studied. The results of a series of such experiments confirmed the findings of previous work by the authors, and supported their hypothesis that the inhibitory effect of morphine on intestinal propulsion was brought about by a prolonged contraction which closed the lumen of the gut and interrupted the normal process of coordinated contractions. This hypothesis appears to reconcile previous apparent contradictions, and indicates that those movements activated by morphine are in reality the cause of the dampening effect of this drug on the intestinal activity. Observations on the action of antagonist drugs showed that adrenaline or noradrenaline will cause relaxation of the intestine after its affection by morphine in moderate doses, but such effect is but brief and is the same as that of raising the pressure of the fluid passing through the loop; it is replaced soon by the original contraction effect of the morphine. Atropine was found to be much more prolonged in its antagonist effect, but was ineffective against large doses of morphine.

The authors refer to the clinical implications of this work. Though the intestinal function does not seem to be abrogated by a true paralytic phenomenon, it is none the less more or less seriously disturbed by morphine, and this side effect is as clinically important, whatever its cause. In the treatment of paralytic ileus morphine may have its place if used early, as its ability to relieve pain and anxiety will be valuable, but continued administration has obvious objections. Here the value of the substitute drugs comes in, and Vaughan Williams and Streeten point out that the threshold of amidone or pethidine required for inhibition of the power of propulsion of the intestinal muscle is below that needed to produce analgesia, although their capacity to relieve pain is not identical. Pethidine is less active in inhibiting intestinal propulsion, but also less effective in relieving pain. Therefore amidone appears to be more useful in a condition like paralytic ileus. This work draws attention to certain pharmacological principles relating to the mode of action of morphine, that drug of necessity which has not really been displaced by its substitutes, and should help to a greater understanding in its use.

[1] *British Journal of Pharmacology*, June, 1951.

ERYTHEMA NODOSUM.

Erythema nodosum seems to be one of the hardy annuals; even as it blossoms on the skin it keeps appearing in the contemporary literature, perhaps as a reminder that it has not reached finality in its significance as a physical sign. It is now regarded as a reaction of the skin to a variety of agents, which may be bacterial or chemical in origin, and thus not truly specific in nature. Since the introduction of the sulphonamides we have been reminded of the potential importance of certain drugs in producing well-known patterns of reactive manifestations in the skin. An interesting observation was made in the Mayo Clinic that within a period of four months three patients were seen who had demonstrable hilar adenopathy with the eruption and who lost all signs of both cutaneous and pulmonary pathological change while they were under surveillance. This induced C. Clifford Johnson, Norman O. Hanson and C. Allen Good to investigate the frequency of this association.[1] Study of the literature reinforced the general view that *erythema nodosum* is a manifestation of sensitivity to certain infections and certain drugs, and it appeared also that preponderance of particular ætiological factors varied with different geographic locations. Thus Wallgren and others in Sweden have found that tuberculosis was the commonest associated condition, but other investigators in America have found that it is at least not common as a cause in adults. The presence of radiographic evidence of enlargement of the hilar glands has, however, been a frequent feature in many series. Studies have also been made of those patients in whom this intrathoracic feature has been evident, and several writers have

[1] *Annals of Internal Medicine*, April, 1951.

recorded that the hilar adenopathy, which might be slight, moderate or well marked in degree, was in a limited proportion of cases the only demonstrable thoracic sign. Of course, as is well known, the sinister association of *erythema nodosum* and pulmonary tuberculosis has been stressed by numbers of authors; a similar association has been noted, too, between this skin lesion and other forms of tuberculous disease. The rheumatic nature of *erythema nodosum* has of recent years receded into the background of medical beliefs, and all observers do not agree that the painful swollen joints seen as part of the syndrome are similar or due to acute rheumatism. Sarcoidosis and coccidiomycosis have also been blamed for producing this type of reaction, and apart from states somewhat resembling tuberculosis there is a variety of miscellaneous conditions which seem to play an ætiological part, such as streptococcal infections. The present writers introduce a new concept. The syndrome generally accepted as characteristic of *erythema nodosum* includes fever, painful nodular erythematous lesions on the shins and forearms, joint pains and the usual febrile malaise, but Johnson, Hanson and Good suggest that the pulmonary signs are part of the general syndrome; others have made a similar suggestion, but have not followed it up.

The authors examined the records of the Mayo Clinic until they could produce details of 100 cases in which there was no doubt of the dermatological diagnosis and in which radiological investigation was carried out. The patients were chiefly female, only 23 being male, and most of them were adults. Eleven patients were tested with tuberculin, but only two reacted. Two had frank tuberculous disease. Of the 100 patients, 30 showed no sign of other associated disease and 20 had an unspecified infection of the upper respiratory tract. The remainder had various conditions, chiefly infective, and it is interesting that 15 were sensitive to drugs which were regarded as the causal agent. Nine patients in this series had radiological evidence of hilar glandular enlargement, and in all but one instance this was bilateral. Five patients were followed up, and in these the shadows seen in the hilar regions disappeared in a period of months. The outcome of this investigation was that no disease state other than *erythema nodosum* was found in nine out of 100 patients with this condition who also had evidence of hilar adenopathy. Therefore, Johnson, Hanson and Good put forward the tentative belief that hilar enlargement may be an associated manifestation of *erythema nodosum* of non-specific ætiology. This does not affect the necessity for cautious inquiry into the possibility of the existence of some important infection, notably tuberculosis; but it would appear that the interpretation of shadows in the pulmonary hilar region in this condition should be at least no more dogmatic than it is at present.

MYOCARDIAL INFARCTION IN DETROIT.

It might be thought that myocardial infarction had been so thoroughly studied that there was not much more to be said about it. But as clinicians as well as statisticians believe that the incidence of this important condition varies in different environments, and have a feeling, if a statistician will permit so vague description of the steps leading to conclusions, that this, the most common type of heart affection today, is connected with the stresses of life. F. Janney Smith, John W. Keyes and Ralph M. Denham have collected a series of 920 patients who suffered from proven attacks of myocardial infarction, drawn from the general population of a very busy industrial city, Detroit, where, as the authors remark, "many people live under stress of production-line working conditions".[1] Perhaps it is appropriate that the patients were studied in the Henry Ford Hospital. The study of the clinical data was made rather more difficult by the fact that the authors did not always have the opportunity of seeing the patients at equally early periods in their illness, but the history, the physical examination, the standard methods of examination in the side room and the laboratory, and the observation of the complications and effects, if any, of intercurrent disease were all studied. The overall mortality in this series was 23·2% and the anterior occlusions were found, as in other series, to be more lethal than the posterior. This was particularly so in women; 92 men out of 353 died following anterior infarction, but 30 out of 74 women. No special seasonal incidence was recorded, nor were there any striking findings concerning occupation, the figures for which would in any case need to be related to the occupational scattering of the urban population. There was no special relation of the mortality to hypertension, and though the incidence of hypertension was greater in the women patients, the death rate was not much raised by this factor.

One important observation, which tallies with that made by others, was the significant number of patients who experienced attacks of angina for periods ranging from a few days to several weeks before the major seizure. This might be of some prophylactic importance; physicians not infrequently see patients with suggestive or equivocal symptoms, the true significance of which may be masked by an electrocardiogram with no special deviations from the average. The present authors were struck by this observation and were led to treat such patients at once by rest in hospital and the administration of anticoagulants; the results will be given later. Obesity did not appear to have any influence *per se* on the mortality rate. The same applied to *diabetes mellitus* and, although other writers have found a higher death rate from myocardial infarction in diabetics, no statistical difference could be demonstrated in the present series. Previous infarction of the heart added considerably to the gravity of the prognosis, as might be expected, and the figures seem to show that this applied particularly to men. No fresh light is shed on the question around which so much controversy has centred, the importance or otherwise of physical or mental stress. Smith, Keyes and Denham found evidence of possible precipitating factors in only 6·5% of the series, and the majority of cases occurred during routine activities or with the patient at rest, either awake or asleep. The factors modifying the prognosis once the attack has occurred were those generally recognized: a high leucocyte count, the site of the infarction, and, in particular, thrombo-embolic complications. With regard to the last named, the overall mortality rate was 42%. Here the effect of anticoagulant therapy may be mentioned. This form of treatment was given to 189 patients, and of these 15, just under 8%, had thrombo-embolic episodes, whereas these occurred in nearly 20% of those who did not receive anticoagulants. The death rate among all patients treated with these preparations was 14%, a figure which is raised by an apparently high rate among women. The authors cannot produce certain evidence of the actual value of anticoagulant treatment in patients who have had preliminary symptoms of angina, but they believe that it has relieved symptoms and helped to prevent imminent infarction.

Numbers of other observations have not been referred to in this review, such as the incidence and treatment of cardiac irregularities and the drug treatment of these and other conditions, but it should be pointed out that the authors found digitalis of benefit for congestive failure and that they found that dicoumarol alone gave results as good as those obtained with heparin. The greater speed attained in control of thrombosis by heparin they considered of value, but they cannot produce evidence that an initial period of administration of heparin improved the results with dicoumarol alone. Perhaps the subject seems well worn, but the importance of premonitory symptoms should be again emphasized and encouragement given for the continued use of an efficient anticoagulant, with the necessary precautions and knowledge of its possible dangers. The full story of the value of this therapeutic method can probably be told only by statistics, and these in turn can be trusted only in measure as the clinical data are correct. The reason for the increase, real or apparent, in the incidence of myocardial infarction has yet to be proved, and here too only controlled experience can give the answer.

[1] *The American Journal of the Medical Sciences*, May, 1951.

Abstracts from Medical Literature.

OBSTETRICS AND GYNÆCOLOGY.

The Rh-Sensitized Patient.

BRUCE B. ROLF (*American Journal of Obstetrics and Gynecology*, January, 1951) stresses the need, in preparation for the management and classification of the Rh-negative patient, to assemble the following facts as a routine from all obstetric patients: (i) complete obstetric and transfusion history, including record of abortions and possible intramuscular injections of blood; (ii) routine Rh factor determinations for all patients in the pre-natal stage including *primiparæ*; (iii) if the patient is Rh negative, results of tests on the children and husband to determine the husband's genotype (homozygous or heterozygous for the Rh factor); (iv) with Rh incompatible mating, further study in the nature of antibody tests. The frequency of the antibody tests depends on the chances the mother has had for being previously sensitized, and the ability to predict the occurrence and severity of erythroblastosis is relative rather than specific. The author states that one survey showed that 45·4% of women with ante-partum sensitization delivered infants with erythroblastosis, one-half of whom died of the disease. Factors in order of importance are (i) blocking antibodies (albumin), higher than agglutinating (saline), (ii) increase in antibodies during the last month before delivery, (iii) appearance of antibodies earlier than ten weeks prior to confinement, (iv) presence of Rh antibodies in all successive testings after their first appearance. The titre does not always bear a relationship to the severity of the disease; however, the higher the titre, the greater the likelihood for stillbirth in the Rh-positive fœtus. Induction of labour before intrauterine death occurs, if the infant is viable, may yield a baby which can be treated, and may be indicated if (*a*) the antibodies increase in the thirtieth to thirty-sixth week, (*b*) there is a history of a previous erythroblastotic baby or of transfusion with Rh-positive blood, or (*c*) the husband may be presumed to be homozygous. An X-ray study of the fœtus *in utero* should be carried out to ensure the presence of a live fœtus, to determine the maturity of the baby and to exclude the possibility of an hydropic baby. Indications for Cæsarean section should be based on adequate obstetric rather than serological findings—the mortality rate in such cases for the fœtus with delivery by Cæsarean section is 50% higher. The delivery should take place in a hospital with full facilities for both maternal and baby transfusion. The cord is doubly clamped several inches from the abdominal wall to allow sufficient for exchange transfusion, if needed. Cord blood is tested as follows: (i) Coombs test—a positive result is considered pathognomonic of the disease and may indicate its severity; (ii) hæmoglobin estimation—the most reliable index of severity in comparison with the maternal or fœtal antibody titres; (iii) Rh group determination and blood typing; (iv) cell count, with examination of a smear for nucleated red blood cells; (v) determination of icterus index—this is optional in the absence of jaundice. The author states that many babies with mild erythroblastosis will survive without transfusion, but it is important that transfusion when indicated should be given as soon as the blood test results are reported. Rh-negative specific type blood from female donors should be used, and multiple transfusions over a month to six weeks may be needed. Exchange transfusion may be decided upon when there is evidence of moderate to severe disease. Reports after two years suggest a lower incidence of brain damage following exchange transfusion. A 10% to 30% incidence of neurological sequelæ, such as mental retardation, athetosis, cerebral palsy, hearing defects and the like, has been reported in children born with erythroblastosis.

Spontaneous Retroperitoneal Hæmorrhage Complicating Pregnancy.

ROBERT W. KISTNER AND STANLEY T. GARBER (*The Western Journal of Surgery, Obstetrics and Gynecology*, January, 1951) report a case of spontaneous retroperitoneal hæmorrhage complicating pregnancy and discuss the condition on an analysis of nine cases reported in the literature during the past thirty years. Their patient was a multiparous woman, aged twenty-nine years, who developed sudden sharp pain in the left hypochondrium after defæcation. She was at about the twenty-sixth week of pregnancy, and her pregnancy had hitherto been normal. The pain increased, and there were signs of shock and collapse without vaginal bleeding, severe tenderness and rigidity in the left flank extending down into the left iliac fossa. A pre-operative diagnosis was made of intraperitoneal hæmorrhage from a varix of the left broad ligament, and laparotomy was performed. A massive hæmorrhage was found between the layers of the broad ligament, extending retroperitoneally to the region of the kidney and spleen. A stab-wound incision was made in the left flank, and 1000 millilitres of blood clot were evacuated. The hæmatoma cavity was then packed with gauze. The patient was tided over a post-operative course of acute illness with frequent blood transfusions and penicillin, streptomycin and sulphadiazine therapy. An analysis of cases reported in the literature prompts the observation from the authors that this condition is a rare and usually fatal complication of pregnancy. In only four of the ten reported cases did the patient survive. The authors state that the condition has been described as occurring as early as the tenth week of pregnancy and as late as twenty-six hours *post partum*. The ætiology remains obscure, and the possibility of multiple causative factors must be considered. Ruptured aneurysm of the renal artery was considered the cause in two cases; ruptured aneurysm of the splenic artery was the cause in one reported case, and rupture of a hæmorrhoidal vein accounted for another case. Thrombosis and capillary bleeding associated with preeclampsia and eclampsia were considered the causes in two cases. Trauma due to intercourse, defæcation or labour was a possible ætiological factor in half the cases. The authors discuss the possibility of hypervitaminosis *A* and hypovitaminosis *C* in the ætiology of the condition. They consider that if pregnancy has passed the fourth month, the general lines of treatment are hysterectomy, exploration of the hæmatoma, evacuation of the hæmatoma and tamponade.

The Dangerous Placenta.

JOHN STALLWORTHY (*American Journal of Obstetrics and Gynecology*, April, 1951) discusses the problems of the placenta, low-lying and attached to the posterior wall of the uterus. He states that the ideal to strive for with *placenta prævia* is a record of no maternal deaths and fœtal wastage of less than 10%. Early diagnosis is essential, and in the author's series 28 patients (16·5%) were admitted prior to the onset of bleeding; 35 (28%) had a malpresentation of major degree. Soft tissue radiography with determination of the head-brim relationship is believed to be nearly 100% accurate in the determination of the placental site; the great value of the method is that it permits of a preliminary selection of those patients in the antenatal clinic suspected of having a *placenta prævia*, and admission to hospital, where expectant treatment is adopted to the thirty-sixth or thirty-eighth week. In any large series it should be possible to admit to hospital at least 20% of women with *placenta prævia* before there is any hæmorrhage; the more cases detected in the antenatal clinic before hæmorrhage occurs, the better will be the result for mother and baby. In 170 cases in which the placental site was confirmed at operation or by digital vaginal examination, 50% of placentæ were posterior in position and out of reach of all but the most experienced fingers; this prevented engagement of the presenting part and rendered difficult or impossible the adequate control of bleeding by the vaginal route. This type I or type II placenta is the "dangerous placenta" with increased risk to the fœtus from cord compression. With the central or type IV placenta there is little dispute in regard to treatment, but the author regards it as much more important to know where the presenting part is in relation to the brim than where the placenta is in relation to the os. If the head cannot be made to enter the brim, Cæsarean section, preferably but not exclusively of the lower segment type, is performed; the incidence was 40% over the whole series, and in the last 100 cases the incidence was 51% with a fœtal wastage of 13·7%. With *placenta prævia* anæmia must be detected early and adequately treated; expectant treatment is possible in over 80% of cases.

The Trend Towards Complete Hysterectomy.

IRVING F. STEIN (*The Western Journal of Surgery, Obstetrics and Gynecology*, January, 1951) states that the trend towards total hysterectomy has been accelerated by the recognized significance of cervical stump disease. Following subtotal hysterectomy, hæmorrhage, pelvic pain, dyspareunia, urinary symptoms and cervical discharge may persist until the cervix is removed. The mortality rates following total hysterectomy in large series of cases from the literature vary from 0·2% to 1·1%. The gynæcological staff of Michael Reese Hospital performed 561 hysterectomies in the year before the writing of the author's paper, 94% being total hysterectomies. The complete operations included 60% of total abdominal and 40% of vaginal hysterectomies. There were no deaths

in this group. The author agrees with other authorities who consider that many hysterectomies are performed unnecessarily chiefly owing to inadequate investigation of the symptoms and signs. He considers that patients with fibroid tumours not causing hæmorrhage or other pelvic symptoms may well be observed over a period of years. Many of these fibroid tumours remain static or undergo involution and atrophy after the climacteric. Carcinoma *in situ* of the cervix and selected cases of very early invasive carcinoma of the cervix are indications for total hysterectomy according to the author. Chronic pelvic inflammatory disease in older women and chronic inflammatory disease which has required previous surgical treatment are also considered as indications for total hysterectomy. For women of lower age groups who suffer from prolapse, the more conservative Manchester operation is preferred by the author to vaginal hysterectomy with repair. He stresses the importance of accurate diagnosis with use of ancillary investigations. He states that hysterosalpingography, posterior colpotomy and culdoscopy are often employed as diagnostic aids, and, in his experience, gynecography with use of pneumoperitoneum has proved to be of the utmost value. He considers that there would be fewer unwarranted hysterectomies if gynecography was used more generally in pelvic diagnosis. Cytological examination has been employed with increasing frequency, but the author considers that biopsy should always be performed in cases of positive or suspicious results from smear examinations. He considers that it is difficult to confirm or refute the argument favouring total hysterectomy for cervical cancer prophylaxis, but total hysterectomy is not warranted as a means of cancer prophylaxis alone.

Fertility and Endometriosis.

William V. Cavanagh (*American Journal of Obstetrics and Gynecology*, March, 1951) reports a statistical study of patients with proven external endometriosis in an attempt to answer questions on the social state of patients who develop endometriosis and on the ætiological roles of late marriage and of too infrequent and late childbearing in this condition. He states that it is well recognized that endometriosis is associated with sterility, but that it is controversial whether endometriosis is a disease of well-to-do women and that it may be due to late marriage and too infrequent childbirth. It has not been fully established whether the lack of pregnancies is a cause or an effect of endometriosis. Among 646 subjects of endometriosis studied, 57% were private patients with an average age of 37·5 years and 43% were ward patients with an average age of 38·3 years. The overall incidence of external endometriosis was found to be 7·5% of all laparotomies for pelvic disease. The author concludes that in the series studied, the incidence of endometriosis was much the same in ward patients as in private patients. An analysis of the series with regard to marital status showed little difference from that reported in the United States census of 1940 for women of all ages above fifteen years. However, endometriosis is slightly more common in unmarried woman after the age of thirty years. The study suggests that endometriosis is associated with infertility in twice the normal expected frequency among women marrying before the age of thirty years and nine times the expected frequency thereafter. A study of ward and private patients with endometriosis in comparison with a control group of women shows no difference in the median age at marriage. The author considers that this shows no tendency of patients destined to have endometriosis to postpone marriage. No tendency was found in future endometriosis patients to delay pregnancy after marriage. The author concludes that the significant reproductive feature of endometriosis patients is the high incidence of sterility, which may as well be the result of the endometriosis as the cause. He states that there is no evidence from this series to show that endometriosis results from voluntary delay of pregnancy or is related to economic conditions.

The Lower Uterine Segment.

Wilfred Shaw and Pushpa Nirula (*The Journal of Obstetrics and Gynæcology of the British Empire*, April, 1951) describe certain anatomical and clinical features of the lower uterine segment and suggest a theory as to its extent and origin. They describe the reflexion of the peritoneum from the front of the uterus to the bladder and record constant histological findings at this site. They state that there is a small fossa on the anterior surface of the uterus, in the mid-line, immediately above the peritoneal reflexion. The apex of this fossa is directed downward. The apex of the fossa is a fixed point, but the fossa may become displaced when the uterus is enlarged or distorted by myomata. There is no precise association between the apex of the fossa and the internal os, but on an average the apex of the fossa corresponds to the level of the internal os. The authors have observed that the fossa is displaced upwards in the direction of the fundus of the uterus even in the early weeks of pregnancy, and by the tenth week of pregnancy the apex of the fossa is about one inch above the level of the anatomical internal os. At term and particularly after labour has commenced, the fossa with the peritoneal reflexion to the bladder is drawn up still more. A study of museum specimens by the authors did not confirm the accepted view that the anatomical internal os is drawn up early in pregnancy, before the eighteenth week. The mucous membrane of the *isthmus uteri* had been studied histologically by the authors and the response to progesterone and the extent of decidual reaction have been noted. They have the impression that stroma decidual cells in the upper part of the isthmus have grown down into the isthmus from the compact layer of the endometrium of the body of the uterus. The lower uterine segment is defined by the authors as that part of the uterus in labour which lies below the physiological retraction ring. They describe two rings in the mucous membrane of the uterus at term, one at the level of the anatomical internal os and the other at the level of the histological internal os; these rings are not necessarily related to the muscle ring of the physiological retraction ring. They believe that the position of the anatomical internal os ring bears a constant relationship to the muscle retraction ring, and that part of the lower segment is formed from the isthmus and part is formed from the lower part of the cervix. The lower edge of the upper uterine segment has a characteristic conical shape, which marks the transition from the condensed muscle tissue of the upper segment to the thin layer of muscle tissue which passes downwards beneath the mucous membrane of the cervix. The apex of this cone is described as being usually situated two-thirds of the way down the *isthmus uteri*. The authors have noted no gross changes in the myometrium around the internal os up to about the twentieth week of pregnancy. Near term the lower part of the uterus above the cervix is distended and stretched by the fœtal head, there is an upward pull of the condensed muscle layer, and the apex of the cone is drawn upward. Clinical investigation by the authors suggests that the internal os retains its position at least until the twentieth week, that the apex of the cone (the lower border of the upper segment) is drawn upwards and that the fœtal head sinks low down into the uterus at about the time of lightening; this explains why the patient feels relief at this time. The authors consider it reasonable to believe that the characters of the condensed muscle layer are determined by the basal layer of the endometrium of the body and by the mucous membrane of the *isthmus uteri*.

Decidual Reactions of the Cervix.

H. E. Bowles and I. L. Tilden (*The Western Journal of Surgery, Obstetrics and Gynecology*, April, 1951) report an incidence of 32·6% of decidual reactions of the *cervix uteri* in 92 consecutive biopsies taken during pregnancy from the cervix and from cervical polypi; 29 of 79 polypi showed decidual reactions and one of twelve cervical biopsy specimens. The authors consider that decidual reaction of the cervix is probably much more frequent as a clinical entity than publications on the subject in American literature would indicate. The 29 cervical polypi with decidual changes showed no unusual clinical findings. The single cervical biopsy specimen with decidual reaction had the clinical appearances of carcinoma of the cervix. The patient was a thirty-eight-year-old Chinese multiparous woman who was eight months pregnant. Examination of the cervix revealed a circumscribed indurated lesion, one centimetre in diameter, on the upper lip of the cervix. Examination of a biopsy specimen taken through the edge of the lesion showed, histologically, a pronounced decidual reaction with much inflammation. The lesion promptly involuted after an uneventful delivery. The authors observe that decidual reactions of the cervix vary in size from three to twenty millimetres in diameter; a covering of stratified squamous epithelium may be present; the epithelial covering is commonly denuded and replaced by a layer of exudate. Associated inflammatory changes are common, and the decidual cells may be typical of those of the endometrium or may show degenerative changes. In two cases the decidual cells were elongated, bizarre and atypical, and resembled decidual reactions observed in areas of endometriosis. The authors consider that recognition of the cervical decidual reaction is important as it may be confused with carcinoma and it may substantiate the diagnosis of pregnancy.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal North Shore Hospital of Sydney, Crow's Nest, New South Wales, on June 21, 1951. The meeting took the form of a series of clinical demonstrations by members of the medical and surgical staff of the hospital. Parts of this report appeared in the issues of September 22 and 29, 1951.

Squamous-Celled Carcinoma of the Kidney.

DR. ALBAN GEE showed a woman, aged eighty-one years, who complained of bleeding from the vagina, of three months' duration. Although she was a trained nurse and realized the significance of this sign, she had done nothing about it—probably because she was almost blind, owing to a cataract of the left eye and to glaucoma of the right eye from which a cataract had been removed. Two days prior to her admission to hospital, she had had severe pain in the left loin, which persisted for six hours. It was relieved by morphine, but recurred the following day with the passage of blood clots. On her admission to hospital, heavy complete hæmaturia was present, for which no cause could be found on clinical examination. The urine was not infected; a blood count gave results within normal limits, except for a slight leucocytosis; the blood urea content was 42 milligrammes *per centum*. An excretion urogram revealed normal renal outlines, and dilatation of the right renal pelvis and calyces, possibly due to pressure by an aberrant vessel on the ureter. The left renal tract could not be seen clearly. Bleeding had ceased by the time cystoscopic examination was made, and the left pyelogram was not helpful. However, four days later, further cystoscopic examination revealed a blood clot protruding from the left ureteric orifice. A catheter was passed easily to the kidney and heavily blood-stained urine was obtained. The pyelogram revealed a dilated pelvis, and the upper calyx was very poorly filled and drawn out. The other calyces and pelvis were clearly defined. It was thought that there was probably a tumour in the upper pole, and this was confirmed at operation. However, on section of the kidney, the tumour was clearly arising from a papillary growth in the pelvis which had invaded the renal substance. Section proved this to be a squamous carcinoma.

Dr. Gee pointed out that that highly malignant tumour was relatively rare, only about 100 cases having been reported in the literature. The chief presenting sign was hæmaturia, commonly with associated pain from the renal tract involved; but often vague gastro-intestinal symptoms and loss of weight were noticed first. Early urological investigation with subsequent nephrectomy offered the patient his only chance of avoiding metastases.

Hydronephrosis in a Horseshoe Kidney.

Dr. Gee's second patient was a man, aged fifty-three years, who had presented with a history of frequency of micturition. This occurred as often as every hour during the daytime, and up to eight times at night. There was slight burning and scalding during the act, but he had a good stream and no hesitancy. There were no symptoms referable to the upper part of the urinary tract. A specimen of urine was found to contain 60 to 80 pus cells per high-power field, and the culture yielded a growth of Gram-negative coliform bacilli which fermented lactose. An excretion urogram demonstrated a horseshoe kidney with normally shaped, medially directed calyces on the right side, but with dilatation on the left side of both pelvis and calyces. A cystoscopic examination disclosed a cyst on the verumontanum, to which diathermy was applied, but there was no abnormality in the bladder, and catheters were passed to both kidneys without difficulty. The indigo-carmine test gave a good blue colour from the right side, but only a pale green colour from the left. Examination of specimens of urine from the bladder and from the left kidney revealed numerous pus cells, and culture produced a growth of coliform bacilli. Urine from the right kidney contained no abnormal features. A left pyelogram was taken, and revealed the presence of a large hydronephrosis with an apparent narrowing of the uretero-pelvic junction. There was also a dilated area in the ureter at the brim of the pelvis. Exploratory operation was advised, with the thought that left nephrectomy and division of the isthmus of tissue joining the two kidneys might be necessary. However, as the patient was not inconvenienced by his condition, he decided to report back only if his symptoms increased.

Crossed Renal Ectopia with Fusion.

Dr. Gee's third patient was a man, aged twenty-nine years, who had suffered attacks of pain in the penis for many years, associated with frequency of micturition, more particularly at night, and some scalding during the act. He had passed blood in the urine when at the age of eight years, and on numerous further occasions until the age of sixteen years. There was no history of renal colic, or of upper abdominal pain. On rectal examination a very hard area could be felt above a normal prostate in the area corresponding to the trigone of the bladder. An excretion urogram revealed the presence of a large oval-shaped bladder calculus, two inches long and one and a quarter inches wide. In addition the two kidneys could be seen to be fused to form a horseshoe kidney of unusual outline, of which only a very small portion appeared to the right of the mid-line. The left renal outline appeared to be normal, but the right appeared to be in the transverse axis across the second and third lumbar vertebræ. At cystoscopic examination, the indigo-carmine test gave a good result on the left side, but only a deep green colour from the right, the ureteric orifices being normal in position. The pyelograms revealed a most unusual state. The left renal outline was normal, though the kidney was a little more laterally placed than usual. There was no actual pelvis, the ureter entering the centre of a channel, one-quarter of an inch wide, running in the length of the kidney, from which on both medial and lateral aspects calyces arose. The right ureter crossed the mid-line over the body of the fifth lumbar vertebra and appeared to enter the collecting system of the right kidney three-quarters of an inch to the left of the lower margin of the third lumbar vertebra. To the left of this there was one large calyx directed downwards along the medial margin of the lower pole of the left kidney, while the remainder of the collecting system ran across the third lumbar vertebra to terminate half an inch to the right of the body. It was about one inch wide, and from it dilated calyces branched above and below. Thus the kidneys formed the shape of the letter "T" lying on its side, with only a small part of the right kidney lying to the right of the vertebral column. The urine from the right kidney contained numerous pus cells, and a growth of coliform organisms was obtained on culture. No surgical treatment was advised, though in view of the inadequate drainage of some calyces, a cure of the infection by the exhibition of antibiotics was not considered likely. The bladder calculus was removed by suprapubic cystotomy, with complete amelioration of the pain and frequency of micturition.

Dr. Gee said that the explanation of how fusion of the kidney took place was not clear; but they knew that ascent of either kidney might be arrested at any point between the second sacral and second lumbar vertebræ, and that normally that ascent took place with the pelvis on the ventral surface rotating medially as it rose. It appeared in that case that the lower pole of the right kidney fused with the medial aspect of the lower pole of the left kidney. That prevented the left kidney from rotating, but its ascent carried the right kidney with it, across and to the left of the mid-line. That followed the usual rule that the kidney assuming the more cranial position determined the side of the body in which both kidneys would lie. The incidence of the condition was not high, less than 200 cases having been reported. It was of interest that the patient had congenital cardiac abnormalities also.

Abnormalities of the Diaphragm.

DR. COTTER HARVEY showed a series of patients illustrating abnormalities of the diaphragm, as follows. (i) Diaphragmatic hernia. (ii) Eventration of the diaphragm. (iii) Artificial pneumothorax complicated by pneumoperitoneum. (iv) Artificial pneumoperitoneum complicated by pneumothorax. (v) Two cases in which the diagnostic aid of pneumoperitoneum had been sought to elucidate the nature of a rounded swelling in relation to the right side of the diaphragm. One proved to be due to a partial eventration of the right side of the diaphragm. The other, in a symptomless male subject, aged eighty-three years, was thought to be a small simple tumour of the liver.

Ganglioneuroma of Posterior Mediastinum.

DR. BRUCE WHITE showed a female patient, aged sixteen years, who had been admitted to hospital on February 27, 1951. For two months she had had a cough, and she had lost weight after an attack of measles. Otherwise she was well, with no sputum, no dyspnœa and no chest pain.

On examination of the patient, the trachea was in the mid-line, there was no finger clubbing and the chest movement was equal on both sides. The percussion note was

hyperresonant posteriorly at the lung base on the left side. Breath sounds were absent on the left side below the level of the fourth thoracic vertebra. Vesicular resonance was absent over the same area. A blood count gave normal results. No acid-fast bacilli were found in the sputum. An X-ray examination of the chest revealed a large tumour lying postero-medially in the left side of the chest. It appeared to rise, not from the lung, but from the mediastinum. The Casoni and complement-fixation tests produced negative results.

Thoracotomy was performed, and a large tumour in the left side of the chest was excised. It was spherical, partly cystic and mainly solid; it appeared to arise from the left sympathetic chain. Microscopic examination showed the tumour to be a ganglioneuroma. The patient was discharged from hospital, cured.

Cyst of the Lung.

Dr. White's second patient, an unmarried woman, aged twenty-two years, had been admitted to hospital on February 13, 1951. She complained of the occurrence of asthmatic attacks for twenty years; they had increased in severity over the preceding two years. Adrenaline and aminophylline had stopped the attacks. Otherwise the patient was symptomless. She had no cough, no sputum, no hæmoptysis, no dyspnœa and no loss of weight.

On examination of the patient finger clubbing was present. The trachea was in the mid-line. Pronounced thoracic kyphosis and prominence of the sternum were present, and chest movement was diminished. The percussion note was hyperresonant on each side of the sternum, more so on the left. Breath sounds were diminished over the hyperresonant area. A blood count gave normal results. The Mantoux test produced no reaction. An X-ray examination of the chest revealed a cyst arising from the anterior margin of the lung, herniating into the anterior mediastinum.

Thoracotomy was performed and the cyst was excised; it was found to contain air and to arise from the anterior margin of the left lung. The cyst was ruptured during its removal. Microscopic examination of the cyst showed the wall to be composed of collapsed lung tissue with no epithelial lining; the diagnosis was simple cyst. Hæmothorax developed, requiring many chest aspirations. A follow-up X-ray examination on March 12 suggested that a further cyst was taking the place of the one already removed. In the lung beneath it were many rounded spaces suggestive of further cysts.

The Use of Physiotherapy in Thoracic Surgery.

Dr. Ian Monk showed patients suffering from a number of surgical conditions of the thorax to illustrate the use of physiotherapy in treatment.

Bronchiectasis.

Dr. Monk's first patient was a male, aged twenty-one years, who in 1948 had coughed blood. In March, 1950, a series of severe hæmoptyses occurred at intervals of approximately two months. The last severe hæmoptysis occurred in January, 1951, the patient's hæmoglobin value falling as low as 9·0 grammes *per centum*. Investigation revealed bilateral bronchiectasis involving the middle and lower lobes of the right lung and the lower and lingular lobes of the left lung. In addition the patient at times coughed up a cupful of thick, purulent sputum.

The patient was in hospital for seven weeks before operation. During that time the greater part of the day and evening was spent in breathing exercises and postural drainage. Just prior to operation he was producing only a trace of mucoid sputum. His average chest expansion had increased by about 0·5 inch to 1·0 inch, as measured at three levels. He was discharged from hospital on the twentieth day after operation, at which left lower and lingular lobectomy was performed.

Traumatic Hæmopneumothorax.

Dr. Monk's second patient, a male, aged sixty-five years, had been admitted to hospital on February 20, 1951. One week previously he had fallen and fractured the seventh, eighth, ninth and tenth ribs. He was admitted to hospital gravely ill and in great pain, breathless in bed and with a temperature of 102° F. He was found to have a hæmopneumothorax with complete atelectasis of the left lung. In addition a parodoxical appearance of the chest wall was noted in the area of the fractured ribs. The assistant surgical registrar injected procaine and "Proctocaine" into the fracture sites, with great relief of the pain; the patient was enabled to breathe with greater freedom, to cough and to be put in a suitable posture. Old blood was aspirated and air was removed from the pleural cavity. During the following few hours the patient was able to cough up several ounces of thick, tenacious, purulent sputum. The lung was rapidly aerated, fever subsided, and the grave danger of a totally infected lung and total empyema was avoided with the use of simple physical methods.

Cystic Bronchiectasis.

Dr. Monk then showed a male patient, aged twenty-four years, who on May 15, 1950, had undergone right pneumonectomy for cystic bronchiectasis throughout the right lung. The indications for pneumonectomy were cough with purulent sputum, and recurrent hæmoptysis. Some six weeks after the pneumonectomy a modified thoracoplasty was performed, in order to prevent undue shift of the mediastinum of the left lung.

Dr. Monk said that the patient had been well and working for over six months, with no disability; he had some chest deformity, but normal arm movements.

Chronic Empyema.

The next patient shown by Dr. Monk was a male, aged twenty-two years, who had been admitted to hospital on March 3, 1950. The patient had had a right *empyema thoracis* drained at the age of ten years, and a further rib resection and drainage performed at the age of sixteen years for a so-called recurrence of the empyema. About a month before his admission to hospital the patient had complained of pain in the chest, and of fever.

On his admission to hospital, flattening and contraction of the right hemithorax were noted, with gross scoliosis, the right shoulder being about three inches lower than the left. Practically no chest movement occurred on the right side.

On March 7 a thick-walled, saucer-shaped empyema cavity about six to eight inches in diameter was drained by resection of three inches of the seventh rib. At operation no expansion of the lung could be seen when the patient coughed. The patient was out of bed on the day after operation, and local and general chest expansion exercises were carried out for the remainder of the patient's stay in hospital, and after his discharge from hospital, which was on March 31, one month after his admission. The drainage tube was not removed until June 21, 1950, the guide to removal being the complete disappearance of the empyema cavity. The patient had returned to work before the final removal of the tube. Dr. Monk commented that the patient's chest had been flattened and immobile for twelve years.

Thoracoplasty for Tuberculosis.

Dr. Monk finally showed a male patient, aged thirty-six years, who had been admitted to the thoracic unit on January 5, 1950, with a tuberculous cavity in the upper lobe of the right lung, which had been present since November, 1946. A three-stage thoracoplasty was performed, with removal of the first and second ribs and of graded amounts of the third to the seventh ribs. At the time of the meeting the patient was well and working.

Dr. Monk commented that the case showed that with attention to posture and to shoulder-scapula movement the patient would have no deformity when dressed, and practically no deformity when unclothed and viewed from the front. The shoulder girdle movements were normal.

Large Penetrating Gastric Ulcer.

Dr. H. Hunter Jamieson showed a woman, aged sixty-five years, who had been admitted to hospital on April 23, 1951. Her history was that she was well until January, 1951, when she developed severe anorexia, particularly in relation to meat, and she began to suffer from attacks of flatulence and discomfort in the epigastrium. The attacks came on at any time of the day or night, were unrelated to meals, and were relieved by "antacid" powders. She had lost three stone in weight and was feeling very weak. On examination, she was very emaciated and pale. There was a palpable mass in the epigastrum, which was very tender on palpation. On vaginal examination a hard round mass was felt in the right fornix; this was thought to be an enlarged right ovary. A blood count revealed a severe degree of anæmia, a fractional test meal examination revealed slight hyperchlorhydria, and a barium meal X-ray examination showed an extensive filling defect of the middle third of the stomach, which was fixed, the appearance suggesting inoperable carcinoma. The patient had a hæmatemesis of approximately half a pint some hours after her admission to

hospital; this was treated by blood transfusion. She received more blood and was fed on a Varco diet for two weeks. On May 10 laparotomy was performed. She was found to have a large ulcer on the lesser curvature of the stomach, which was penetrating the liver anteriorly and the pancreas posteriorly. The stomach was freed from these organs, and subtotal gastrectomy performed. The pelvic mass was found to be a calcified fibroid tumour. The patient was fed by the intravenous drip method and by Ryle's tube for three days post-operatively. She received penicillin, streptomycin and ascorbic acid. Her progress was satisfactory, her wound healed well, and at the time of the meeting she was able to take small, frequent meals without discomfort.

Cardiospasm.

Dr. Jamieson's second patient, a single woman, aged fifty-eight years, had been admitted to the Royal North Shore Hospital of Sydney on May 1, 1951. For twenty years she had had difficulty in eating solid food, which seemed to "stick" at the level of the xiphisternum for some hours. The symptom almost disappeared at times, but recurred whenever the patient was under nervous stress. In December, 1950, the condition had become accentuated (she was having housing difficulties), and she began to suffer dull pain over the xiphisternum after meals. On examination, she was a well-nourished woman; there were no relevant physical findings. Œsophagoscopy was performed, and the lower half of the œsophagus was seen to be very dilated. No ulcer or malignant change was seen. X-ray examination with the swallowing of a barium bolus also revealed the grossly dilated œsophagus. On May 10, 1951, Heller's operation was performed through a thoracic approach. About six inches of the left sixth rib were removed, and the left pleural cavity was opened. The œsophagus was narrow for one inch above the diaphragm, and above this it was very dilated. The longitudinal and circular muscle fibres of the œsophagus were divided longitudinally for a length of one and a half inches above the diaphragm, and the mucosa immediately bulged through the incision. A drainage tube was left in, and the pleura and chest wall were closed. Breathing and supportive coughing exercises were started as soon as the patient regained consciousness, and large doses of penicillin were given. The patient was fed by intravenous drip administration and by Ryle's tube for four days. She was then able to take a light diet without discomfort, and clinically her condition appeared to be much improved.

Malignant Tumour of Left Tibia.

Dr. Jamieson then presented a married woman, aged thirty-four years, who had been admitted to the Royal North Shore Hospital of Sydney on March 27, 1951. In November, 1950, she had received a blow on the upper end of the left tibia, and ever since that time had suffered recurring attacks of pain in the same area; the pain was sharp and stabbing, came in waves every two or three weeks, and lasted three or four days. She had had short-wave therapy with no effect. X-ray examinations in January and February, 1951, had shown no osseous lesion, but X-ray examination on March 27 had shown an area of "quiet osteolysis" in the upper tibial metaphysis. The patient had an irregular fever, up to 100° F., and a diagnosis of subacute osteomyelitis was made. Penicillin therapy was commenced. X-ray examination on April 9 showed that the lesion had extended, and administration of "Chloromycetin" was also started. On April 14 the leg became very painful and swollen, and a further X-ray examination showed that the lesion had extended. The radiologists were now of the opinion that the lesion was a malignant neoplasm—probably secondary. Complete physical and radiological examination failed to reveal the presence of any other neoplasm, and on April 19 some friable material was removed from the upper end of the left tibia for microscopic examination. The condition found in the section was very difficult to classify, but was thought to be either secondary carcinoma or a localized lesion of leuchæmia; so on April 26 the left thigh was amputated ten inches below the greater trochanter. The pathologist's report stated that the tumour was anaplastic; it could be secondary carcinoma, Ewing's tumour or reticulum cell sarcoma. Dr. Jamieson said that the patient had made a good convalescence; "nerve twitchings" and "phantom pains" had been relieved by tapping the exposed nerve endings in the stump. There was no sign as yet of any metastases, and deep X-ray therapy had been considered unnecessary by the honorary X-ray therapist.

Carcinoma of Prostate Presenting as Hypoglossal Nerve Palsy.

Dr. Jamieson's last patient, a man, aged sixty-five years, had been admitted to hospital on May 15, 1951. He had suffered anorexia for six months and had lost three stone in weight; he had also had "fibrositis" of the lumbar region and had had nocturia for years. One month before admission to hospital he had retired to bed quite well, but awoke some hours later and found that he was unable to protrude his tongue. That condition had persisted unchanged. On examination, he was seen to be an obese man with no sign of weight loss; the left half of his tongue was paralysed. There was no evidence of a lesion of the other cranial nerves, and the rest of the nervous system appeared to be intact. On rectal examination the prostate was found to be enlarged and very hard, with small hard nodules palpable as part of the gland. There was no other relevant physical finding. An X-ray examination of his skull revealed irregular areas of osteolysis suggestive of metastasis, but there was no lesion in the remainder of his skeleton. The serum acid phosphatase value was 12·4 units. A diagnosis of carcinoma of the prostate was made, and it was assumed that the paralysis of the left twelfth cranial nerve was caused by one of the metastases in the skull. The patient was given stilbœstrol therapy, commencing at 45 milligrammes daily for three weeks, then 30 milligrammes daily for two weeks and then 15 milligrammes daily. On May 31 subcapsular bilateral orchidectomy was performed. It was considered that as yet it was too early to see any definite results from the treatment.

Osteoclastoma of Sacrum.

DR. L. S. LOEWENTHAL presented a youth, aged seventeen years, who had been admitted to hospital on March 7, 1951. His history was that he had fallen on his left buttock, but was able to limp home. From that date he complained of persistent pain, which did not increase or decrease in the following weeks. Two weeks after his injury he became obstinately constipated and had to have an enema every second day. His limping became gradually worse, but still affected only the left lower limb. For two weeks prior to his admission to hospital he complained of paræsthesia in the perineum and left buttock and down the back of the left thigh; that gradually became worse. On examination, the patient was found to walk with a limp to the left. There was limitation of flexion and external rotation of the left hip due to pain. There was no sensory loss, and all reflexes were normal. Rectal examination revealed a mass attached to the sacrum posteriorly; it was not tender. X-ray examination revealed a soft-tissue mass quietly eroding the sacrum. All other investigations failed to reveal any abnormality. While the patient was in hospital, sigmoidoscopy was performed, and the posterior rectal wall was seen to be bulged forward by a mass from which blood was aspirated. An anterior extraperitoneal approach was made to the sacrum, and a mass was seen to be attached to the sacrum. Biopsy showed only blood cells and voluntary muscle fibres. Later a posterior approach was made and a cavity in the sacrum curetted. This time some giant cells were seen in the sections examined, and a diagnosis of osteoclastoma was made. After curettage the patient's symptoms gradually decreased, and he was discharged from hospital to have deep X-ray therapy.

Carcinoma of Ampulla of Vater.

DR. ERIC GOULSTON presented a man, aged forty-five years, who had been admitted to hospital in September, 1949, with a history of painless, intermittent jaundice for eight months, with clay-coloured stools, dark urine, loss of weight and lassitude. On admission to hospital, the patient was very jaundiced, but otherwise in apparently good condition. His appetite was good, flatulence was slight; he was not upset by fatty foods, had vomited only three times in nine months and was almost normal in weight. The liver edge was just palpable. There was slight tenderness and guarding over the gall-bladder area. Otherwise the results of physical examination were negative. Biochemical tests indicated obstructive jaundice. No gall-stones were seen radiologically. Laparotomy was decided on. Pre-operative treatment included administration of vitamin *K* and blood transfusion. At operation carcinoma of the ampulla of Vater was found. (The diagnosis was later confirmed histologically.) The duodenum and head of the pancreas were removed. The common bile duct was anastomosed to the jejunum. End-to-side gastro-jejunostomy was performed Drainage tubes were left in the gall-bladder and paracolic gutter. Post-operative treatment included intravenous administration of serum, blood and dextrose-saline solution;

also the exhibition of bile salts, "Synkamine", pancreatin, ascorbic acid, "Vibex" and methionine. Convalescence was marked by development of a pancreatic fistula and a period of vomiting. The patient was free of both these complications, and was ambulatory, three weeks after operation. He was discharged from hospital having a special diet including pancreatin. Dr. Goulston said that in February, 1950, the patient's local doctor had reported that the patient was quite symptomless, had a good appetite and digestion, and had gained about two stone in weight.

(To be continued.)

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

GOVERNOR KING TO LORD HOBART.[1]

[*Historical Records of Australia*, May 9, 1803.]

My Lord,

. . . . . .

Whilst I am on this subject, I beg to call Your Lordship's attention and humanity to the situation of the rising offspring of the inhabitants as the smallpox has never been introduced or occurred here.[2] From the frequent cargoes of convicts from England, the introduction of the infection in the natural way is to be expected, and its ravages will be dreadful, happen when it will. To your Lordship's discernment I beg to suggest the idea of the vaccine matter being sent out in every possible manner by a whaler, but not to be sent on board until the ship is on the eve of departure from England. Her voyage may not be more than four months which may ensure its efficacy. Every search has been made on the teats of our cattle, but nothing of the kind can be found. Indeed no cattle are more free from any distemper.

. . . . . .

I have, &c.,
PHILIP GIDLEY KING.

Medical Practice.

PHARMACEUTICAL BENEFITS ACT REGULATIONS.

THE attention of medical practitioners is drawn to the following amendments to the Pharmaceutical Benefits Regulations, which came into force on August 31, 1951.

1. REGULATION 12: Supply of benefits upon prescriptions.

Regulation 12 has been amended so as to provide that the person obtaining the pharmaceutical benefit must sign and date a receipt for it on the back of the prescription form, and an approved pharmaceutical chemist, approved hospital authority, or approved medical practitioner shall not supply a pharmaceutical benefit upon presentation of the original copy of the prescription unless this is done.

The Regulation is further amended so as to permit a medical practitioner to write on an authorised prescription form a prescription for the supply of the following pharmaceutical benefits in two or more different strengths, viz.:

Aurothioglucose (Oily),

Calcium Aurothiomalate,

Pertussis Vaccine,

Sodium Aurothiomalate (Aqueous),

Sodium Aurothiomalate (Oily).

2. REGULATION 13: Prescriptions not to be written on prescription forms in certain cases.

Regulation 13, which provides that a medical practitioner treating a person in or at an approved public hospital shall not write a prescription in respect of that treatment on an authorised prescription form, has been repealed.

3. REGULATION 14: Prescribing of certain drugs in short supply.

Regulation 14, which provides that a medical practitioner shall not write on an authorised prescription form a prescription for the supply of a pharmaceutical benefit to which this Regulation applies (drugs in short supply) unless the Director-General of Health or his Delegate has given the practitioner a numbered authority so to write the prescription, has been repealed and a new Regulation substituted in lieu thereof.

The new Regulation provides that a medical practitioner shall not write on an authorised prescription form a prescription for the supply of a restricted pharmaceutical benefit unless he writes on the prescription form, in relation to the prescription, the words: "I certify that in my opinion there is no other drug available which would be equally effective in this case."

The amended Regulation, however, further provides that where deemed necessary by the Minister, a medical practitioner shall not write on an authorised prescription form a prescription for the supply of a particular pharmaceutical benefit unless the Director-General or a Delegate of the Director-General has given to him a numbered authority so to write the prescription and he refers, on the form, to that authority and its number.

(N.B. The first part of the amendment refers to drugs in short supply such as Aureomycin, Streptomycin and Chloramphenicol. The second part of the amendment will no doubt apply to A.C.T.H. or Cortisone if and when they are included as pharmaceutical benefits.)

A new Regulation, 14A, provides that the Minister for Health may by notice published in the Government Gazette, declare that a pharmaceutical benefit specified in the notice may be prescribed only for the treatment of a disease specified in the notice. While a notice under this Regulation is in force in relation to a pharmaceutical benefit a medical practitioner shall not write on an authorised prescription form a prescription for the supply of that pharmaceutical benefit unless,

(*a*) that pharmaceutical benefit is required for the treatment of the disease specified in relation to that pharmaceutical benefit in the notice,

(*b*) he writes on the prescription form, in relation to the prescription, the words "written in accordance with Regulation 14A".

(This Regulation will not become operative until such time as the drugs envisaged, e.g., those for the treatment of carcinoma of the prostate, Parkinsonism, etc., have been included in the Second Schedule to the Regulations.)

4. SECOND SCHEDULE TO THE REGULATIONS:

The Second Schedule (i.e., Commonwealth Pharmaceutical Formulary) has been amended as follows:

(*a*) by inserting after Item 11 (Aureomycin) the following Item:

11A	Aurothioglucose (oily)	—	0·01 G. amp.	1	3
		—	0·025 G. amp.	1	3
		—	0·05 G. amp.	1	3
		—	0·1 G. amp.	1	3
		0·01 G. per c.c.	10 c.c. vial	1	—
		0·1 G. per c.c.	10 c.c. vial	1	—

(*b*) by omitting Item 80 (Kinetin) and inserting in its stead the following Item:

80	Kinaden	—	set containing 3 amps. each of 10 units and 3 amps. of solvent	1	1

(*c*) by inserting after Item 131 (Procaine Hydrochloride in Normal Saline) the following Item:

131A	Procaine penicillin (aqueous)	—	300,000 U. vial	6	—
			900,000 U. vial	6	—
			3,000,000 U. vial	6	—

(*d*) by inserting after Item 167 (Sulphonamides Mixed (C)) the following Item:

167A	Suprarenal cortex extract	200 γ per c.c.	10 c.c. bottle	3	1

(*e*) in accordance with the Schedule to these Regulations.

[1] From the original in the Mitchell Library, Sydney.

[2] This suggests that there was still some doubt as to the exact nature of the epidemic which had killed approximately 50% of the natives in the vicinity of Port Jackson.

Correspondence.

PRE-BRONCHIECTASIS.

SIR: I read with interest the article by Dr. H. B. Harwood (THE MEDICAL JOURNAL OF AUSTRALIA, August 25, 1951) in which he stresses the need for early active treatment of lung infection in children as a major step towards the prevention of bronchiectasis. Anyone whose work brings him into frequent contact with this disease would wholeheartedly support any measure designed to prevent its occurrence. As Dr. Harwood indicates, the responsibility of initiating treatment falls on the general practitioner, but it is unfortunate the medical profession in general shows such a lack of interest in the ætiology and pathology of bronchiectasis that it is unable to contribute much to its prevention and treatment.

Dr. Harwood's summary of the pathology, predisposing causes, symptoms *et cetera* should be read by all who come in contact with sick children, but his conclusions as to methods of treatment are in my opinion erroneous.

His contention that the bronchoscope is the complete answer to the problem of pre-bronchiectasis, and reversible bronchiectasis, is not shared by many authorities. He quotes freely from that classical series of articles by Elaine Field, but omits the section where she concludes that: "Unless foreign body is suspected, immediate bronchoscopy is no longer considered necessary. No significant difference in the incidence of re-expansion of the lung was found between the cases treated by bronchoscopy and those treated without." And again: "Bronchoscopy was not helpful in diagnosis and localisation of bronchiectasis." (The collapse she refers to is that which, when associated with infection, is the main ætiological factor in bronchiectasis.)

When one considers the very ætiological factors which Dr. Harwood lists in his paper, it is difficult to see how bronchoscopy performed at intervals of three or four weeks can do much to alter the *status quo*.

It must be admitted that the aspiration of secretion, and the coughing that can be encouraged by bronchoscopy, is better than no treatment at all. However, it seems more reasonable to place increased reliance on postural drainage, steam inhalations and breathing exercises, carried out daily under the direction of a specially trained physiotherapist, and repeated more frequently at home under parental control.

Such treatment is more rational because it is repeated several times a day, and is, therefore, constantly attacking the problem.

It is unfortunate that Dr. Harwood chooses 50 selected cases to illustrate his contention, because such a series loses its significance without the background of all cases treated in the same period of time.

In spite of my disagreement with the treatment with which his paper is concerned, I would like to support Dr. Harwood's plea for early recognition and treatment of pre- and reversible bronchiectasis, and, thereby, preventing the development of irreversible established disease.

Yours, etc.,

170 North Terrace,
Adelaide,
September 11, 1951.

H. D'ARCY SUTHERLAND.

POISONING FROM A "BENZEDRINE INHALER".

SIR: The following personal experience may be of interest to readers and may expose an unsuspected danger.

My son, just two years old, was bathed one evening, and when being fed half an hour later, his mother noticed that he seemed excited and "naughty". Some four hours later, when I arrived home, his condition was most alarming—the main points being constant screaming, continuous restlessness, dilated pupils and some thirst, but no desire for food. The hands were pulled down across the neck alternately, and when put down the child ran about rapidly—always on tip-toe!

The case was a bit puzzling, but his sister told of seeing him suck water out of a "Benzedrine Inhaler" in the bath, and the finding of a waterlogged inhaler clinched the diagnosis.

Small (and inadequate) doses of morphine and phenobarbital were given with little effect, and the symptoms persisted unabated for eighteen hours. The thumb was so violently sucked that quite a deep wound resulted. He was then given one and a half grains of phenobarbital intramuscularly and went to sleep for eighteen hours. Stimulation returned, and a further small injection was required. It was fifty-four hours before the child had returned to normal.

As these inhalers when fresh contain over 300 milligrammes of active principle, it can be seen that a poisonous dose could readily be extracted from even one "free sample".

Yours, etc.,

Hobart,
Tasmania,
September 20, 1951.

C. A. DUNCAN.

MORTALITY FROM CONGENITAL MALFORMATIONS IN AUSTRALIA.

SIR: I wish to comment on one aspect of my friend H. O. Lancaster's article on "Mortality from Congenital Malformations in Australia" (THE MEDICAL JOURNAL OF AUSTRALIA, September 8, 1951, page 318). In comparing the tendency of different forms of congenital malformation to affect males more than females he lays some stress on the marked "masculinity" of the deaths from congenital pyloric stenosis and "imperforate anus". He acknowledges the possible fallacy in arguing from death rates in such cases, and would, I suppose, admit that it may be that more males die of these conditions than do females, despite effective treatment.

Whereas in the case of congenital pyloric stenosis all would agree that the male stands an equal chance with the female as regards recovery, I believe there is good reason to expect females born with "imperforate anus" to recover more often than males. The reason is that not all cases of "imperforate anus" have a complete blockage of the bowel. Many are relieved from danger of early death by the presence of a reasonably efficient fistulous track which allows fæces to be excreted, and it is well known amongst pædiatric surgeons that the female infant with imperforate anus frequently has a recto-vaginal or perineal fistula which works fairly well, but the male infant less frequently has a recto-urethral or recto-vesical fistula, and even if he does it is not adequate as an escape route for fæcal excretions.

Ladd and Gross ("Abdominal Surgery of Infancy and Childhood") give figures for Boston Children's Hospital from 1908 to 1939 for "imperforate anus or an associated abnormality" which show an equal incidence in either sex. However, out of 107 female cases 70 had a fistulous safety valve to the vagina or perineum, but out of 107 male cases only 48 had such a safety valve, of which only 20 were to the perineum. It is obvious that more males than females will require urgent surgery in the newborn period, and that many of the females but few of the males may continue to survive without any treatment whatever.

Conclusions based solely on figures require the primary hypothesis that contrasted groups of cases are as nearly as possible "similar in all respects", and I feel that in this particular instance Dr. Lancaster has failed to establish that primary hypothesis.

Yours, etc.,

123A Miller Street,
North Sydney,
September 24, 1951.

E. S. STUCKEY.

Post-Graduate Work.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

PROGRAMME FOR NOVEMBER.

Week-End Refresher Course at Hamilton.

A WEEK-END refresher course will be held at Hamilton in the 3HA theatrette on November 17 and 18, 1951. The programme will be as follows:

Saturday, November 17: 2.30 p.m., Dr. Norman James, "Advances in Anæsthesia"; 8 p.m., Dr. T. Lowe, "The Management of Œdema".

Sunday, November 18: 10.15 a.m., Dr. E. E. Dunlop, "Surgery of the Biliary Tract"; 11.30 a.m., Dr. B. L. Stanton, "New Drugs and Prescribing Problems".

The fee for this course is £2 2s. or 10s. 6d. per demonstration. Enrolments should be made with Dr. S. C. Fitzpatrick, 69 French Street, Hamilton. Telephone 190.

Lecture at Flinders Naval Depot.

Dr. Leslie Hurley will conduct a demonstration on thyreotoxicosis at Flinders Naval Depot on November 14, 1951, at 2.30 p.m. by arrangement with the Royal Australian Navy.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1945, as duly qualified medical practitioners:

Brandstater, Bernard John, M.B., B.S., 1951 (Univ. Adelaide), 58 Porter Street, Parkside, Adelaide.

Whitney, Ormond Andrew, M.B., B.S., 1946 (Univ. Melbourne), Chanter Street, Berrigan.

Bedingfeld, Richard Collier, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Wellington.

Bradley, Edgar David, M.B., B.S., 1951 (Univ. Sydney), Maitland Hospital, West Maitland.

Champion, Maret, M.B., B.S., 1951 (Univ. Sydney), 36 Victoria Road, Bellevue Hill.

Conley, Valda Mary, M.B., B.S., 1951 (Univ. Sydney), Tweed District Hospital, Murwillumbah.

Cook, Samuel West, M.B., B.S., 1951 (Univ. Sydney), Prince Henry Hospital, Little Bay.

Crane, Henry Graham Elliott, M.B., B.S., 1951 (Univ. Sydney), 20 Nicholson Street, Burwood.

Cull, Francis William, M.B., B.S., 1951 (Univ. Sydney), c.o. Dr. Calnan, Ballina.

Doutreband, Allan Roy, M.B., B.S., 1951 (Univ. Sydney), 5 Culdees Road, Burwood.

Fisher, Adrian Welby, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Armidale.

Friendship, Colin James, M.B., B.S., 1951 (Univ. Sydney), 387 Bronte Road, Waverley.

Gage, Harold Thomas, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Griffith.

Gillespie, James Albon, M.B., B.S., 1951 (Univ. Sydney), 96 Ashley Street, Chatswood.

Goldman, Sonia, M.B., B.S., 1951 (Univ. Sydney), Rachel Forster Hospital, Redfern.

Grieve, Neil McLean, M.B., B.S., 1951 (Univ. Sydney), 329B Rainbow Street, Coogee.

Grossy, Moses, 15 Plowman Street, North Bondi. Registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1950.

Higgins, Ivy Patricia, M.B., B.S., 1951 (Univ. Sydney), 18 Solander Street, Kogarah.

Lester, Vincent, 17 Harriette Street, Neutral Bay. Registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1950.

Locke, Gerald Macmillan, M.B., B.S., 1951 (Univ. Sydney), Maryborough Hospital, Queensland.

Low, Bruce, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital of Sydney, St. Leonards.

Mayne, Robert John Bruce, M.B., B.S., 1951 (Univ. Sydney), Waterfall Sanatorium, Waterfall.

Meldrum, William Arthur, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Lithgow.

Nield, James Marland, M.B., B.S., 1951 (Univ. Sydney), 14 Cambridge Road, Drummoyne.

Northcott, Geoffrey Charles, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Goulburn.

O'Connor, James Keith, M.B., B.S., 1951 (Univ. Sydney), 5 Lennox Street, Mosman.

Pitsch, Werner Jobst, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Parkes.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 8, 1951.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Ankylostomiasis	•	1	..	..	..	..	..	..	1
Anthrax	•	..	..	..	..	..	..	..	..
Beriberi	•	•	•	•	•	•	..	•	..
Bilharziasis	•	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	4(3)	3(1)	..	..	1	..	..	..	8
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	•	•	..	•	•	•	•	•	..
Dengue	•	•	•	•	•	•	..	•	..
Diarrhœa (Infantile)	..	..	11(10)	..	..	..	..	..	11
Diphtheria	6(2)	..	4(1)	4(4)	7(5)	..	..	..	21
Dysentery (Amœbic)	•	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	•	2(2)	..	..	..	..	..	2	4
Encephalitis Lethargica	..	2	..	..	..	..	..	..	2
Erysipelas	•	•	•	..	•	•	..	..	..
Filariasis	•	..	..	..	..	..	..	..	..
Helminthiasis	•	..	•	•	•	•	•	•	..
Hydatid	•	..	•	•	..	•	..	..	..
Influenza	•	•	•	..	•	•	..	•	..
Lead Poisoning	•	•	..	•	•	•	•	•	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	•	..	..	..	1(1)	..	..	..	1
Measles	•	•	•	97(76)	•	•	..	..	97
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	22(8)	5	6(2)	34(28)	2	..	..	..	60
Psittacosis	•	..	•	..	•	•	•	•	..
Puerperal Fever	..	..	1	..	..	..	..	..	1
Rubella(*c*)	•	11(9)	..	•	8(1)	•	..	1	20
Scarlet Fever	17(14)	15(6)	3(1)	10(10)	6(3)	1(1)	..	..	52
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	•	..	..	•	•	•	•	•	..
Trachoma	•	..	•	•	•	•	•	•	..
Tuberculosis(*d*)	32(23)	7(4)	16(6)	12(10)	5(5)	3(1)	..	..	75
Typhoid Fever(*e*)	..	..	1	..	..	..	..	..	1
Typhus (Endemic)(*f*)	..	..	..	..	..	..	..	..	..
Undulant Fever	..	..	..	..	..	..	..	..	..
Weil's Disease(*g*)	•	•	1	•	•	•	•	•	1
Whooping Cough	•	•	•	1	•	•	..	..	1
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37 1946-1947. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from the Northern Territory.
• Not notifiable.
(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Saad, Ronald Shalhoub, M.B., B.S., 1951 (Univ. Sydney), Brentwood Hospital, Muswellbrook.
Spencer, Terence Edward Thornton, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Casino.
Strang, Raymond Rattray, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Wollongong.
Tidswell, Thomas, M.B., B.S., 1951 (Univ. Sydney), 29 Musgrave Street, Mosman.
Banyard, Geoffrey Derek, M.R.C.S. (England), L.R.C.P. (London), 1948, 10A Russell Street, Vaucluse.
Jeffrey, George Pearson, M.B., Ch.B., 1945 (Univ. Edinburgh), c.o. Dr. W. Begg, Wauchope.
McCay, Harold Lindsay, M.B., B.S., 1941 (Univ. Melbourne), Gerringong.
Maclaren, Margaret Graham, M.B., Ch.B., 1940 (Univ. Glasgow), 90 Drumalbyn Road, Bellevue Hill.
Ryall, Charles Vaughan Phayre, M.B., Ch.B., 1935 (Univ. Belfast), 16 Keston Avenue, Mosman.

The following additional qualifications have been registered:

Bear, Colin Leslie (M.B., B.S., 1940, Univ. Sydney), 405 Marrickville Road, Marrickville, D.D.M., 1951 (Univ. Sydney).
Bennett, Winston Noel Chevalier Gerard (M.B., 1942, Univ. Sydney), 167 Moulder Street, Orange, B.S., 1947 (Univ. Sydney).
Bray, Sylvia Dean (M.B., B.S., 1929, Univ. Sydney), 18 Laycock Street, Neutral Bay, D.M.R. and E., 1936 (Univ. Cambridge).
Burfitt-Williams, Grosvenor Charles Thomas (M.B., B.S., 1946, Univ. Sydney), 175 Macquarie Street, Sydney, Dip. Ophth., R.C.S. (England), 1950.
Clarke, Arthur John Robert (M.B., B.S., 1947, Univ. Sydney), Marlborough House, Morpeth, D.G.O., 1951 (Univ. Dublin).
Hill, James Allan (M.B., B.S., 1938, Univ. Sydney), 8 Longueville Road, Lane Cove, D.G.O., 1951 (Univ. Sydney).
Laycock, John Field (M.B., B.S., 1944, Univ. Sydney), 31 Cross Street, Concord, D.D.R., 1950 (Univ. Sydney).
Macdonald, Roderick Hector (M.B., Ch.M., 1923, M.S., 1938, Univ. Sydney, F.R.A.C.S., 1938), 135 Macquarie Street, Sydney, M.R.C.O.G., 1950.

TASMANIA.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Act*, 1918, as duly qualified medical practitioners:

Evans, Hughes Peter, M.B., B.S., 1947 (Univ. Melbourne), Repatriation Department, Hobart.
Stanbury, Pauline Marjorie, M.B., B.S., 1950 (Univ. Melbourne), c.o. Department of Public Health, Tasmania.
Sibthorpe, Gwenyth, M.B., B.S., 1946 (Univ. Adelaide), T.D.D., 1950 (Cardiff).

University Intelligence.

UNIVERSITY OF MELBOURNE.

Elections to University Council and to Standing Committee of Convocation.

NOMINATIONS are invited from graduates of the University of Melbourne for election to the University Council and to the Standing Committee of Convocation. The five sitting members of the Council, who were elected in 1947, are due for retirement by effluxion of time on December 17, 1951. They are Dr. J. R. Darling, Mr. C. M. Gilray, Sir Russell Grimwade, the Honourable Sir Charles Lowe and Sir John Newman Morris. For the Standing Committee of Convocation, 21 vacancies fall due on the same date representing graduates in arts (seven), medicine (three), science (three), engineering and architecture, law, commerce (two each), dental science, agricultural and veterinary science (one each).

Sitting members may be renominated. Nominations must be made in proper form, available from the Registrar, with whom nominations close not later than 12 noon on Saturday, October 13, 1951.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Burns, Robert John, M.B., B.S., 1950 (Univ. Sydney), Women's Hospital, Crown Street, Sydney.
Carrick, Denise Myles, M.B., B.S., 1951 (Univ. Sydney), 2 Merlin Street, Roseville.

The undermentioned has been elected a member of the Tasmanian Branch of the British Medical Association:

Nally, Patrick James Francis, L., L.M., 1943, R.C.P. (Ireland), L., L.M., 1943, R.C.S. (Ireland), Ouse, Tasmania.

Diary for the Month.

OCT. 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
OCT. 9.—New South Wales Branch, B.M.A.: Organization and Science Committee.
OCT. 12.—Queensland Branch, B.M.A.: Council Meeting.
OCT. 16.—New South Wales Branch, B.M.A.: Medical Politics Committee.
OCT. 17.—Western Australian Branch, B.M.A.: General Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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